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In the Supreme Court of the United States

MAYO COLLABORATIVE SERVICES (D/B/A MAYO MEDICAL LABORATORIES) AND MAYO CLINIC ROCHESTER,

Petitioners,

v.

PROMETHEUS LABORATORIES, INC.,

Respondent.

Petition for a Writ of Certiorari to the United States Court of Appeals for the Federal Circuit

PETITION FOR A WRIT OF CERTIORARI

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QUESTION PRESENTED

The Federal Circuit, reversing the district court, upheld Prometheus's patent claims covering a process for correlating the level of certain chemicals in a patient's blood with the patient's health. By those claims, Prometheus seeks to monopolize the use of blood tests in the research, diagnosis, and treatment of disease, such that a physician violates the patent merely by thinking about the correlation between the test results and the patient's health or treatment. This Court granted certiorari to determine whether basic scientific relationships may be monopolized in this way in *Laboratory Corp. of Am. Holdings* v. *Metabolite Labs., Inc.*, 548 U.S. 124, 135 (2006) ("*LabCorp*"), but dismissed the writ for lack of adequate issue preservation. Dissenting from dismissal, Justices Breyer, Stevens, and Souter explained that such patents are invalid under this Court's precedents, and that resolving the issue presented in *LabCorp* was of great importance to innovative scientific inquiry and effective medical research and treatment.

The question presented is as follows:

Whether 35 U.S.C. § 101 is satisfied by a patent claim that covers observed correlations between patient test results and patient health, so that the claim effectively preempts all uses of these naturally occurring correlations.

RULES 14.1(b) AND 29.6 STATEMENT

All parties are identified in the caption of this petition. Petitioner Mayo Collaborative Services, a subsidiary of Mayo Clinic, is a for-profit Minnesota corporation that provides reference laboratory services under the name Mayo Medical Laboratories. Petitioner Mayo Clinic Rochester, a subsidiary of Mayo Clinic, is a charitable, nonprofit corporation located in Rochester, Minnesota. No publicly held company owns 10% or more of the stock of either petitioner.

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PETITION FOR A WRIT OF CERTIORARI

Petitioners, Mayo Collaborative Services (d/b/a Mayo Medical Laboratories) and Mayo Clinic Rochester (collectively, "Mayo"), respectfully petition for a writ of certiorari to review the judgment of the United States Court of Appeals for the Federal Circuit.

OPINIONS BELOW

The court of appeals' opinion (App., *infra*, 1a-25a) is reported at ___ F.3d ___, 2009 WL 2950232 (Fed. Cir. 2009). The district court's opinion (App., *infra*, 26a-59a) is reported at 2008 WL 878910 (S.D. Cal. Mar. 28, 2008).

JURISDICTION

The court of appeals entered its judgment on September 16, 2009. The jurisdiction of this Court is invoked under 28 U.S.C. § 1254(1).

STATUTORY PROVISIONS INVOLVED

"Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title." 35 U.S.C. § 101.

"The term 'process' means process, art or method, and includes a new use of a known process, machine, manufacture, composition of matter, or material." 35 U.S.C. § 100(b).

INTRODUCTION

This Court previously granted certiorari on the issue presented in this case in *Laboratory Corp. of America Holdings* v. *Metabolite Laboratories, Inc.*, 548 U.S. 124, 135 (2006) ("*LabCorp*"), but could not resolve the merits because petitioner there had not preserved the issue. The patent claims in *LabCorp* and Prometheus's claims here both attempt to exclude the public from using the results of basic human metabolic testing in the research, diagnosis, and treatment of disease. They do so by claiming protection for the process of recognizing a correlation between the level of certain chemicals in the patient's blood and the patient's health. In both cases, the claims are silent as to what should be done with such correlations and as a result purport to cover and thus preempt all possible uses of the biological correlations.

Applying this Court's case law invalidating patent claims that preempt all uses of a fundamental scientific principle, the three Justices who dissented from the dismissal of *LabCorp* as improvidently granted reasoned that the claims at issue were obviously invalid and not even "at the boundary" of patentability. The district court here reached the same conclusion with respect to Prometheus's claims. The Federal Circuit reversed without even considering the reasoning in *LabCorp*, using a newly minted "machine or transformation" test in place of this Court's established standards for patentability.

This Court should review the Federal Circuit's erroneous decision, which is inconsistent with this Court's precedent and with the reasoning of three Justices in *LabCorp*. As reflected in the grant of certiorari in *LabCorp*, the 20 amicus filings in that

case, and the seven amicus filings in the Federal Circuit here, the issue is one of exceptional public importance. Justices Breyer, Stevens, and Souter explained that "special public interest considerations" are implicated by the question presented because overbroad patents will "inhibit doctors from using their best medical judgment," "force doctors to spend unnecessary time and energy to enter into license agreements," "divert resources" from healthcare tasks to "the legal task of searching patent files," and "raise the cost of health care while inhibiting its effective delivery." 548 U.S. at 138. These considerations again warrant this Court's review, which may now proceed without the problems that prevented resolution in *LabCorp*.

STATEMENT

A. Prometheus's Sweeping Patent Claims

Prometheus's broad patent claims attempt to turn a physician's thought processes into infringement. Specifically, the claims encompass a physician's mental determinations when evaluating a patient who has been given a thiopurine drug.[1] Enzymes in the human body metabolize such drugs naturally into metabolites that are therapeutically active. App., *infra*, 41a. Low levels of such metabolites indicate an insufficient dose of the drug, whereas high levels indicate too much. These facts have been understood by physicians for decades, as the Prometheus patents concede. See, *e.g.*, '623

[1] U.S. Patents 6,355,623 ("the '623 patent") and 6,680,302 ("the '302 patent"), reproduced at C.A. App. A10001 and A10019, are also available at http://tiny.cc/y867p and http://tiny.cc/TR2FY, respectively.

Patent at 8:37-39, C.A. App. A10010 (citing "[p]revious studies" that concluded "measurement of 6-MP metabolic levels can be used to predict clinical efficacy and tolerance" to thiopurine drugs).[2]

What the Prometheus patents purport to add to the art is a recognition that *particular metabolite levels* correlate to proper drug dosages for certain gastrointestinal disorders. App., *infra*, 2a-3a; '623 Patent at 8:40-46, C.A. App. A10010. Those correlations already existed in the studied patient population; Prometheus simply looked at the data for that population to "discover" the levels. App., *infra*, 41a-42a; C.A. App. A12833-12836, A13330-13331.

Claim 46 of the '623 patent, for example, describes such a correlation review process. The sole step in that process involves recognizing the relevance of certain metabolite levels (known as 6-thioguanine (6-TD) or 6-methyl-mercaptopurine (6-MMP)):

> 46. A method of optimizing therapeutic efficacy and reducing toxicity associated with treatment of an immune-mediated gastrointestinal disorder, comprising:
>
> (a) determining the level of [6-TD] or [6-MMP] in a subject administered a drug selected from

---

[2] See also '623 Patent at 9:13-14, C.A. App. A10011 (relevant metabolite levels "can be determined by methods well known in the art"); C.A. App. A12698-12701, A12705-12712, A12714-12718 (scientific papers from 1982-1990 describing tests for relevant metabolite of thiopurine); *id.* at A12722-12727 (1989 article discussing "acute thiopurine toxicity"); *id.* at A12842-12844 (conceding prior testing for thiopurine metabolites).

> the group consisting of 6-mercaptopurine, azathioprine, [6-TD], and [6-MMP], said subject having said immune-mediated gastrointestinal disorder;
>
> wherein the level of [6-TD] less than about 230 pmol per $8x10^8$ red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject, and
>
> wherein the level of [6-TD] greater than about 400 pmol per $8x10^8$ red blood cells or a level of [6-MMP] greater than about 7000 pmol per $8x10^8$ red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.

C.A. App. A10018; see App., *infra*, 3a-5a (describing patent claims at issue). With their technical terms stripped away, Prometheus's claims cover a physician's observation that a test result shows a metabolite level below 230, between 230 and 400, or above 400—*i.e.*, his mental recognition of a natural correlation between metabolite level and patient condition following administration of a drug. See App., *infra*, 3a.

Importantly, Prometheus's claims do not recite what is to be done once the physician recognizes the correlation. App., *infra*, 38a-39a. As a result, the claims cover and preempt *all* such uses. They begin and end with observation of the test results. What the physician might do with that observation is irrelevant because simply thinking about the subject suffices to infringe the patent. As Prometheus's expert testified, if the physician reads an email with the test results, it would not matter if she "crumples

it up, throws it away, reads it, acts on it, doesn't act on it, any assumptions you want to come up with." C.A. App. A13557-613558; see also C.A. Supp. App. A13805-13806. The physician infringes the moment she recognizes the correlation.

Prometheus confirmed the broad scope of its claims when it opposed Mayo's argument in the district court that the claims should be construed to require that physicians actually do something with their knowledge before they could be deemed to infringe—*e.g.*, adjust a dosage level for the patient. C.A. App. A12245-12249. Prometheus successfully argued that the physician would only have to identify a potential need to adjust dosage and denied that the physician must actually adjust the dosage or do anything else. See App., *infra*, 84a-86a.

The extraordinary breadth of Prometheus's patents is made evident by Prometheus's infringement accusations against Mayo researcher Dr. Rokea el-Azhary. Dr. el-Azhary is a dermatologist and therefore unconcerned with metabolite ranges for gastrointestinal disorders. She administered a thiopurine drug to her dermatological patients to see if she could *establish* a therapeutic range for skin disorders. See C.A. App. A12846. But because the lab report she received referred to the correlation ranges in Prometheus's claims, Prometheus accused Dr. el-Azhary of infringement:

> The Biochemical Genetics Laboratory at Mayo Clinic Rochester sent a report of test results to Dr. el-Azhary, or someone working for Dr. el-Azhary. The test results described the "therapeutic range" as "235-400." The Biochemical Genetics Laboratory at Mayo Clinic Rochester did not subsequently advise

> Dr. el-Azhary that the "therapeutic range" was not "235-400."
>
> Such information informed Dr. el-Azhary, or someone working for Dr. el-Azhary (and thus "indicated a need"), that the next dose of azathioprine given to the patient should be increased in order to be within the "therapeutic range."

C.A. App. A12788; A12821-12822. Prometheus even asserted infringement when Dr. el-Azhary subsequently received reports that did not list the "therapeutic range"—on the ground that the ranges were then in her memory. *Id.* at A12853-12854 ¶ 5.

Dr. el-Azhary testified that she knew the numbers, but that metabolite levels relevant to gastrointestinal conditions were "irrelevant to [her] study" because she was researching metabolite correlations in dermatology, not in inflammatory bowel disease, and "there is no reason to extrapolate to dermatology." C.A. App. A12848-12850. Under Prometheus's view of its patents, however, Dr. el-Azhary cannot resume her dermatological research unless and until she rids her memory of the correlations that Prometheus observed in gastrointestinal patients, regardless of how she ultimately may use any test results. She infringes whenever she recognizes the correlations, no matter what else she thinks or does.

In the courts below, Prometheus attempted to gloss over its accusation against Dr. el-Azhary by pointing out that it sued Mayo and not Dr. el-Azhary. But the el-Azhary episode dramatically highlights the broad range of medical research that Prometheus has preempted with its patents. By targeting Dr. el-

Azhary's thoughts, Prometheus can effectively stop her from determining appropriate ranges for her own dermatology patients, because she cannot definitively stop thinking about the metabolite correlations on which Prometheus's patents are based. Anyone who has read Prometheus's patent claims, or any summary of them—including readers of this petition—is similarly disabled. That Prometheus did not name Dr. el-Azhary as a defendant misses the point. If Prometheus were right that she has infringed its patents, any owner of a patent with similar claims could sue a physician in Dr. el-Azhary's position for infringement simply for thinking "forbidden" thoughts. The patent laws were never meant to impose such intolerable consequences.

B. The District Court's Decision Invalidating The Patents

In 2004, Prometheus filed a patent infringement claim against Mayo after Mayo developed and proposed to sell a test to measure metabolites in patients treated with thiopurine drugs that used different levels from those included in Prometheus's patents. App., *infra*, 61a-62a. Construing Prometheus's patent claims in accordance with their broad language, the district court granted Prometheus summary judgment on its infringement claim. *Id.* at 86a-93a.

After the district court permitted the parties to amend their pleadings, Mayo filed a motion for summary judgment contending that Prometheus's patents were invalid. The court granted Mayo's motion, at the same time denying Prometheus's motions for summary judgment on infringement and patent exhaustion. See App., *infra*, 28a-30a (describing procedural history).

In invalidating Prometheus's patent claims under 35 U.S.C. § 101, the district court relied on this Court's case law deeming patent claims invalid if they wholly preempt all uses of a natural phenomenon or abstract idea. App., *infra*, 36a-39a, 42a, 48a-54a. The court started by determining that the Prometheus claims recite correlations between thiopurine drug metabolite levels and therapeutic efficacy or toxicity. *Id.* at 38a-39a. The court rejected, as form over substance, Prometheus's argument that the claims recite "methods" rather than natural phenomena. Looking at the steps of the claims, the court explained that the steps reciting "administering" a drug and "determining" metabolite levels were mere data-gathering steps that were necessary precursors for reviewing the claimed correlation. *Id.* at 39a. In summarizing the claims, the court noted: "what the inventors claim to have discovered is that particular concentrations of [thiopurine metabolites] correlate with therapeutic efficacy and toxicity in patients taking AZA drugs." *Ibid.*

The court then ruled that the correlations are natural phenomena. Rejecting Prometheus's argument that the correlations could not be natural because thiopurine is a synthetic drug, the court observed that Prometheus's claims are directed to the correlation and not to the making of the drug. Prometheus's expert had admitted that "the key therapeutic aspect of such thiopurine drugs is that they are converted *naturally* by enzymes within the patient's body to form an agent that is therapeutically active." App., *infra*, 41a. Prometheus also admitted that the testing and correlations already existed in a "data-base of patient's information" that included patients taking 6-MP drugs, and that the correlations likely still exist in the current patient

population. *Ibid.* As a result, the court concluded (*id.* at 42a), Prometheus

> did not "create" the correlation between thiopurine drug metabolite levels and therapeutic efficacy and toxicity. Instead, the correlation results from a natural body process, which as the inventors concede, was pre-existing in the patient population, and it exists in the patient population today.

In analyzing Prometheus's claim, the district court found instructive the opinion of Justices Breyer, Stevens, and Souter in *LabCorp*. The district court quoted approvingly the *LabCorp* dissenters' explanation that the similar patent claim at issue there failed "the requirement that it not amount to a simple natural correlation, *i.e.*, a 'natural phenomenon'" (citing this Court's precedents):

> At most, respondents have simply described the natural law at issue in the abstract patent language of a "process." But they cannot avoid the fact that the process is no more than an instruction to read some numbers in light of medical knowledge. One might, of course, reduce the "process" to a series of steps, *e.g.*, Step 1: gather data; Step 2: read a number; Step 3: compare the number with the norm; Step 4: act accordingly. But one can reduce *any* process to a series of steps. The question is what those steps embody. And here, aside from the unpatented test, they embody only the correlation between homocysteine and vitamin deficiency that the researchers uncovered. In my view, that correlation is an unpatentable "natural phenomenon," and I

> can find nothing in [the claim] that adds anything more of significance.

LabCorp, 548 U.S. at 137-138 (citation omitted), quoted at App., *infra*, 43a-44a.

Finally, applying this Court's precedents to the record before it, the district court held that the Prometheus claims preempt a natural phenomenon. It first noted that the governing test was not a "transformation/results" test, because this Court had utilized a preemption test in *Gottshalk* v. *Benson*, 409 U.S. 63 (1972), and had invalidated a claim in *Parker* v. *Flook*, 437 U.S. 584 (1978), under the preemption rule without ever mentioning that test. App., *infra*, at 49a-50a. Then, applying the preemption rule, the court held that Prometheus's sweeping claims improperly preempt all uses of the correlations. *Id.* at 51a-54a. That ruling followed from the court's earlier determination that every other activity described in the claims, apart from recognition of the correlation, is a data gathering step necessary to make the correlation (*id.* at 51a):

> what the inventors claim to have discovered is that particular concentrations of 6-TG and 6-MMP correlate with therapeutic efficacy and/or toxicity in [patients] taking AZA drugs. Because the claims cover the correlations themselves, it follows that the claims "wholly pre-empt" the correlations.

C. The Federal Circuit's Decision Upholding The Patents

The Federal Circuit reversed. It glossed over Justice Breyer's *LabCorp* opinion in a footnote, describing it as non-binding but never dealing with its synthesis of controlling law. While noting that the

Prometheus claims addressed different blood tests from those in *LabCorp*, the court of appeals did not come to grips with the fact that *both* sets of claims purport to cover a mental correlation between patient metabolite levels and patient health.

Instead of applying this Court's "preemption" test, as the district court had done, the Federal Circuit applied its own "machine or transformation" test from *In re Bilski*, 545 F.3d 943 (Fed. Cir. 2008) (en banc), cert. granted, 129 S. Ct. 2735 (2009). The Federal Circuit began by calling its "machine or transformation" criterion a "definitive test," and ended by declaring that it replaces the preemption standard:

> [B]ecause the claims meet the machine-or-transformation test, they do not preempt a fundamental principle.

App., *infra*, 24a.

Prometheus invited that ruling by insisting in its briefing that "a freestanding preemption inquiry is inappropriate" because "*Bilski's* 'machine or transformation test is the singular test for a process claim under § 101.'" Prometheus Reply Br. at 21 n.3 (Fed. Cir. Apr. 24, 2009) (quoting *In re Ferguson*, 558 F.3d 1359, 1365 (Fed. Cir. 2009)). The Federal Circuit ultimately focused only on *Bilski* and its own "machine or transformation" test—mentioning this Court's decisions principally through citations to the *Bilski* opinion. App., *infra*, 9a-10a, 15a, 18a. Thus, the Federal Circuit has effectively rendered this Court's preemption test meaningless by making its own "machine or transformation" test controlling.

REASONS FOR GRANTING THE PETITION

By making its "machine or transformation" test the definitive test for patentability under Section 101, the Federal Circuit assumes that a process that involves a machine or transformation cannot possibly preempt all uses of a fundamental scientific principle. That ruling conflicts with this Court's precedents. This Court has utilized the preemption standard as a freestanding criterion, has found preemption without ever asking whether an invention involves a machine or transformation, and has deemed the presence of a machine or a transformation a mere "clue" to patentability. Like the claims in *LabCorp*, the Prometheus claims do not come close to escaping the preemption prohibition. The Federal Circuit's ruling should accordingly be reversed.

I. THE FEDERAL CIRCUIT'S ELEVATION OF ITS "MACHINE OR TRANSFORMATION" TEST TO THE SINGLE DETERMINANT OF PATENTABILITY CONFLICTS WITH THIS COURT'S PREEMPTION STANDARD.

A. The Court has long invalidated patent claims that attempt to preempt all uses of a natural phenomenon.

Although Section 101 is expansive in its reach—covering "anything under the sun that is made by man," *Diamond* v. *Chakrabarty*, 447 U.S. 303, 309 (1980)—it also is subject to important limits. In particular, a patent claim cannot preempt, either directly or by practical effect, a law of nature, natural phenomenon, or abstract scientific idea. As *Chakrabarty* observed:

> [A] new mineral discovered in the earth or a new plant found in the wild is not patentable

> subject matter. Likewise, Einstein could not patent his celebrated law that $E=mc^2$; nor could Newton have patented the law of gravity. Such discoveries are 'manifestations of * * * nature, free to all men and reserved exclusively to none.'

Id. at 309 (quoting *Funk Bros. Seed Co.* v. *Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948)). As the Court has also noted, "[p]henomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work." *Gottschalk* v. *Benson*, 409 U.S. 63, 67 (1972).

This exception to patentability applies not only to a patent claim that is aimed directly at a natural phenomenon, but also to one whose "practical effect would be a patent on the [phenomenon] itself," because such a claim "wholly pre-empt[s]" all uses of the natural phenomenon. *Benson*, 409 U.S. at 71-72. Thus, where a claim recites a law of nature or biological principle, a court must look to whether the claim seeks protection for the phenomenon "in the abstract" or instead implements the phenomenon "in a structure or process which, when considered as a whole, is performing a function which the patent laws were designed to protect." *Diamond* v. *Diehr*, 450 U.S. 175, 191 (1981).

B. Prometheus's claims are invalid because they preempt all uses of the natural correlation between patient metabolite levels and patient health.

The Prometheus claims, like the *LabCorp* claims, recite a natural phenomenon—the correlation between certain metabolite levels and patient health.

That correlation is dictated by natural enzymatic activity inside the human body. As Prometheus's own expert admitted, the drugs are "converted *naturally* by enzymes within the patient's body" into metabolites, as the district court found. The Federal Circuit did not disturb that finding by the district court.

The Prometheus claims preempt all substantial uses of the correlations. In particular, the claims end with the step of recognizing the correlation, and thus cover *anything* that a physician might do with her knowledge of the correlation. Prometheus's expert confirmed the preemptive effect of the claims by testifying that a physician who receives test results that identify the claimed ranges will infringe regardless of what she does with the information—even if she crumples up the test result and throws it away, and regardless of whether or not she acts upon it. C.A. App. A13557-613558; see also C.A. Supp. App. A13805-13806.

The preemptive impact of Prometheus's claims is particularly severe because they are centered on human thought that involves, in any medical context, metabolite ranges that Prometheus observed in patients who took gastrointestinal drugs. Thus, dermatologist Dr. el-Azhary cannot stop thinking about Prometheus's ranges now that she knows of them, even if her goal in reviewing a patient's test results is to find entirely different numbers relating only to dermatology. As a result, Prometheus has obtained a monopoly in a very broad field of medical practice. The preemptive scope of the Prometheus claims is unprecedented. It constitutes an embargo on research and analysis essential to the development of medical knowledge and patient care.

This Court's decisions in *Benson*, *Flook*, and *Diehr* explain the governing preemption standard. In *Flook* and *Benson*, the claims were invalid because they recited a computation but not what was to be done with the computation, thereby covering all its uses. In *Diehr*, the claim recited both a computation of an algorithm and a real-world physical action to be performed with the computation, thus leaving open the possibility that others could make noninfringing uses of the computation. Because it was so limited, there was no preemption. The claims in *Benson* recited a computation for converting numbers from one form to another, but did not recite what was to be done with the numbers once they were converted. Hence, the patent covered all such uses of the idea and would wholly preempt the underlying mathematical formula. 409 U.S. at 71-72. In a like manner, the claims in *Flook* recited a process for updating an alarm limit for use in a chemical process, but never recited what was to be done with the computation even though the claims did recite some "post-solution activity." 437 U.S. at 590. Because the claims covered all uses, they, like the claims in *Benson*, were held invalid.

By contrast, the claims in *Diehr*, which recited use of the Arrhenius equation, also recited a particular application of the equation: using the output of the equation to determine when to open or close an injection mold. In distinguishing that situation from *Benson* and *Flook*, the Court explained (450 U.S. at 187) that

> respondents here do not seek to patent a mathematical formula. Instead, they seek patent protection for a process of curing synthetic rubber. Their process admittedly

> employs a well-known mathematical equation, but they do not seek to pre-empt the use of that equation. Rather, they seek only to foreclose from others the use of that equation in conjunction with all of the other steps in their claimed process.

Prometheus's claims are like those in *Benson* and *Flook* and unlike those in *Diehr*. Claim 46, quoted above, involves nothing more than a physician's recognition of a natural correlation that is part and parcel of a patient's own natural metabolic processes. The claim is not limited to a particular real-world use of that recognition, such as requiring that the physician actually change the dosage after recognizing the correlation. Rather, the claim preempts *all* possible uses of the correlation and thus effectively monopolizes the natural correlation itself.

Prometheus's claims are invalid for the reasons set forth in the opinion of Justices Breyer, Stevens, and Souter in *LabCorp*. In *LabCorp*, the claims were directed to a method of "correlating" a blood homocysteine level with a deficiency in folate, just like the correlation between metabolites and patient condition in the Prometheus claims. Hence, "[t]here can be little doubt that the correlation [is] a 'natural phenomenon.'" 548 U.S. at 135. Like the claims in *LabCorp*, Prometheus's claims simply characterize the use of the correlation as a process, which was plainly insufficient in *LabCorp*:

> At most, respondents have simply described the natural law at issue in the abstract patent language of a "process." But they cannot avoid the fact that the process is no more than an instruction to read some numbers in light of medical knowledge. * * *

> [H]ere, aside from the unpatented test, [the steps in the claim] embody only the correlation between homocysteine and vitamin deficiency that the researchers uncovered. In my view, that correlation is an unpatentable "natural phenomenon," and I can find nothing in [the claim] that adds anything more of significance.

Id. at 137-138. Prometheus's claims fail for the same reason.

Prometheus's central argument in the courts below was that thiopurine is a man-made, not natural, drug (whereas the drug in *LabCorp* was naturally occurring). But as the district court recognized, Prometheus's claims are directed to the correlation and not the drug itself (which Prometheus did not invent). And that correlation results from the body's natural metabolism of the drug. In short, Prometheus cannot take advantage of a drug that was invented by someone else, when its claims are exclusively directed to observing the human body's process of metabolizing the drug—a process that occurs naturally in the human body.

Granting patent protection here simply because Prometheus used a man-made drug would be inconsistent with this Court's invalidation of the patent claims in *Funk Bros.* There, the inventor discovered that certain bacteria could be isolated, mixed together so as not to inhibit each other's properties, and thereby serve as a crop inoculant. 333 U.S. at 130. The Court held the claims invalid because the inventor did not "create" the "state of inhibition or of non-inhibition in the bacteria," but instead "[t]heir qualities are the work of nature." *Ibid.* Of course the claimed combination of bacteria

was man-made. But the inventor had not created the natural phenomenon that was central to the invention. Likewise, Prometheus did not "create" any correlation between metabolite levels and drug efficacy or toxicity, because those correlations were pre-existing in the tested patients, have been observed and analyzed by physicians in their patients for decades, and exist today with or without Prometheus's patents.

In short, the Prometheus patent claims preempt a broad field of scientific thought and research. They seek to monopolize a scientific principle in a manner that is forbidden by this Court's patent preemption rulings. The Federal Circuit's decision conflicts with those rulings and should be reversed.

C. The Federal Circuit improperly applied its "machine or transformation" test in place of this Court's preemption standard.

The fundamental error in the Federal Circuit's resolution of this case was its replacement of this Court's "preemption" standard with its own "machine or transformation" test. As shown above, this ruling is at odds with settled precedent of this Court. In addition, the elevation of the rigid "machine or transformation" test to conclusive status is erroneous and exceptionally harmful.

First, although the Federal Circuit in *Bilski* claimed to find support for its test in this Court's decisions in *Benson*, *Diehr*, *Flook*, and *Cochrane* v. *Deener*, 94 U.S. 780 (1876), those opinions do not say that "machine or transformation" is a dispositive test for patentability or a substitute for the preemption standard. For example, the portion of *Benson* cited

by the Federal Circuit simply says that a transformation or reduction of an article to a different thing is "the clue" to patentability of a method claim that does not involve a particular machine. 409 U.S. at 70. A clue is a guide, not a definitive test.

In any event, the Prometheus claims do not result in any transformation. The only transformation cited by the Federal Circuit was a natural transformation that had already occurred in the patient population that Prometheus studied before it even looked at the test results. The transformation envisioned by *Benson* and other cases is a transformation that makes particular use of the natural phenomenon, and thus prevents the claim from preempting all possible uses. Likewise, the claims in *Diehr* were found patentable, not because a physical transformation was associated with them, but because the claims were limited to a narrow and particular use of the Ahhrenius equation—opening and closing a plastic mold. 450 U.S. at 187.

The Federal Circuit's decision draws even less support from the other two cases on which it relied in *Bilski*—*Flook* and *Cochrane*—because those cases make no mention of such a test. The *Flook* claims involved calculations performed using a computer (a machine) and included a transformation of an "alarm limit" that signaled the presence of abnormal conditions during catalytic conversion. 437 U.S. at 585-586. The Court nevertheless found the claims invalid because this transformation was insignificant "post-solution" activity that did not alter the fact that the claim was directed at a "mathematical formula" for updating alarm limits. *Id.* at 593-595. While the Court observed in a footnote that an "argument can be made" that the Court has affirmed

process claims only when the process "either was tied to a particular apparatus" or operated to change materials to a "different state or thing" (*id.* at 588 n.9), *Flook* did not adopt such a position. Even that possible "argument" made "machine or transformation" a minimum requirement, not a definitive test for patentability.

Likewise, in *Cochrane*, the Court simply noted that a process "is a mode of treatment of certain materials to produce a given result," and "an act, or a series of acts, performed upon the subject-matter to be transformed and reduced to a different state or thing." 94 U.S. at 788. It did not identify either "machine" or "transformation" as a test, let alone *the* test, for patentability. By their omission of any "machine" or "transformation" analysis, these two cases confirm that "machine or transformation" is not the definitive standard for patentability under Section 101.

Shutting its eyes to this Court's preemption standard, the Federal Circuit observed that giving a drug to a patient was "'central to the purposes of the claimed process.'" App., *infra*, at 10a; see *id.* at 20a. But the court overlooked the fact that giving the drug was simply a preparatory data-gathering step for the ultimate correlation and did not limit the use of the correlation in any manner. The court also misperceived the relevance of any "transformation." If the transformation limits the claim to a particular real-world use of the fundamental principle, it can be supportive of patentability. But if it is merely a preparatory data-gathering step—leaving the rest of the claim open to preempt all uses of the principle—it does not make an otherwise unpatentable claim patentable. Thus, whether or not a patient receives a

thiopurine drug (a drug not invented by Prometheus), none of Prometheus's claims is limited in any manner: they cover anything done with knowledge of the natural correlation.

In the end, the "machine or transformation" test appears to be another effort by the Federal Circuit to fashion an inflexible standard that is unmoored from Congress's purposes in enacting the patent laws. This Court repeatedly has rebuffed such interpretations in recent years. For example, in *KSR Int'l Co.* v. *Teleflex, Inc.*, 550 U.S. 398, 418 (2007), the Court faulted the Federal Circuit for establishing an inflexible "teaching, suggestion or motivation to combine" standard that did not comport with the underlying rationale set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1 (1962), and other precedents. In *Medimmune, Inc.* v. *Genentech, Inc.*, 549 U.S. 118 (2007), the Court was critical of the Federal Circuit for adopting an inflexible rule for declaratory judgment jurisdiction, where that rule was unmoored from the underlying "case or controversy" requirement. And in *eBay Inc.* v. *MercExchange, L.L.C.*, 547 U.S. 388 (2006), the Court faulted the Federal Circuit for applying an inflexible injunction standard that did not address the full range of underlying equitable considerations. The Federal Circuit's adoption of a rigid "machine or transformation" standard here, which allows Prometheus to preempt a broad field of scientific thought and research, is equally indefensible.

II. CERTIORARI SHOULD BE GRANTED TO RESOLVE THE IMPORTANT QUESTION LEFT UNRESOLVED IN *LABCORP*.

The Court should grant review rather than hold the petition for *Bilski*. As the government empha-

sized in *Bilski*, that case turns on whether Bernard Bilski's invention is the sort of "technology" that should properly be protected by a patent. *E.g.*, U.S. Br. in *Bilski*, No. 08-964, at 8 (issue in *Bilski* is whether "methods of organizing human activity that are untethered to technology" are "technological and industrial processes" eligible for protection under Section 101). The resolution of that case will not decide the independent question raised here—whether an invention preempts a scientific idea by covering all uses.

This Court has already found the issue presented here to be certworthy in *LabCorp*. This case is an appropriate vehicle to resolve the important issue left undecided there for lack of issue preservation. The Prometheus invention is easy to understand and centered on a plain natural phenomenon. The Section 101 issue was the only issue raised on appeal, and it was addressed directly and extensively by the Federal Circuit and the district court. And because the Federal Circuit has exclusive jurisdiction over patent appeals from district courts (28 U.S.C. § 1295), erroneous decisions such as this one have immediate nationwide impact. Accordingly, this Court often grants review of Federal Circuit rulings based on the importance of the issue presented to the interpretation and application of the patent laws. *E.g.*, *Merck KGaA* v. *Integra Lifesciences I, Ltd.*, 545 U.S. 193 (2005). Such review is especially warranted here because the Federal Circuit's analytical error is fundamental and will be repeated if not corrected by this Court.

Furthermore, the question presented is one of extraordinary public importance at the heart of the patent laws. The critical need for this Court to

resolve that issue now is evidenced by the extensive amicus participation both in *LabCorp* and in the Federal Circuit in this case. Many amici stressed that patents like Prometheus's impede improvements in healthcare, drive up costs, and freeze innovation, as the dissenting Justices in *LabCorp* also recognized (548 U.S. at 138):

> [S]pecial public interest considerations reinforce my view that we should decide this case. To fail to do so threatens to leave the medical profession subject to the restrictions imposed by this individual patent and others of its kind. Those restrictions may inhibit doctors from using their best medical judgment; they may force doctors to spend unnecessary time and energy to enter into license agreements; they may divert resources from the medical task of health care to the legal task of searching patent files for similar simple correlations; they may raise the cost of health care while inhibiting its effective delivery.

These adverse consequences are profound given the sweep of the Federal Circuit's ruling and extend far beyond gastrointestinal disorders. If Prometheus can obtain a patent on correlations between drug administration and the resulting biological reactions in the human body, and prevent medical researchers and providers from thinking about those correlations in different ways, a host of medical entrepreneurs will claim patent monopolies on blood tests with the same preclusive consequences. A patent claimant could seek, for example, to monopolize the correlation between administration of anticoagulant drugs and chemical reactions in the blood, asserting that

these reactions are "man-made" phenomena, and thereby preclude improvements in this commonplace and essential form of medical care.

Therapeutic drug monitoring is fundamental to safely and effectively treating a variety of patient disorders with medication. Mayo, and physicians throughout the world, routinely measure metabolite levels in patients being treated with an array of drugs, including those for the treatment of epilepsy, heart arrhythmias, and depression. Therapeutic monitoring is also central to medicines used in the treatment of organ transplant and cancer patients. Improvements in the administration of all these life-saving drugs would be curtailed if patent claimants could assert a monopoly over every use of metabolite or other therapeutic correlations.

In this very case, Mayo sought to adjust the metabolite reference range deemed relevant by Prometheus to achieve more accurate results and improved patient care. App., *infra*, at 61a; Mayo Mem. in Support of Summary Judgment, filed Mar. 17, 2005, at 5-6 (Dkt. No. 15). But Prometheus blocked that innovation by asserting that it infringed Prometheus's exclusive right to specify relevant biological correlations.

The harmful impact of overly broad intellectual property protection on innovation is also of more general concern for the U.S. economy. Academic commentary confirms that allowing patents to preempt important fields, like medical diagnosis, by monopolizing scientific laws, would greatly increase costs and retard innovation. See M. Boldrin & D. Levine, AGAINST INTELLECTUAL MONOPOLY 73-77, 89-92, 184-187, 214-218, 238, 246 (2009) (describing dramatic increase in patent grants over last decade

resulting in a "patent thicket" harmful to innovation); L. Lessig, THE FUTURE OF IDEAS 205-217 (2001) (describing negative impact of broad patent protection on innovation; "we should be most concerned when existing interests use the legal system to protect themselves against innovation"); W. Landes & R. Posner, THE ECONOMIC STRUCTURE OF INTELLECTUAL PROPERTY LAW 305-306 (2003) (patent monopolies on "scientific principles" threaten "enormous potential for rent seeking" and "enormous transaction costs that would be imposed on would-be users"); R. Merges & R. Nelson, *On the Complex Economics of Patent Scope*, 90 COLUM. L. REV. 839, 915 (1990) ("[T]he real threat of a patent like this stems from the industry's close ties to science. * * * The Patent Office and courts should not permit the over-privatization of the scientific knowledge that makes the industry possible"); L. Branstetter, *Do Stronger Patents Induce More Local Innovation?*, 7 J. INT'L ECON. L. 359, 369 (2004) ("well-structured research projects conducted by competent scholars" have "failed to find" innovation benefits from expanded patent monopolies); A. Torrance & B. Tomlinson, *Patents and the Regress of Useful Arts*, 10 COLUM. SCI. & TECH. L. REV. 130, 138, 162-167 (2009) (collecting economic research showing lack of stimulus to innovation from broad patent grants).

At a minimum, and especially at this time of paramount national concern over health care costs and quality, this research shows "that a heavy burden of persuasion should be placed upon those who would extend such protection." S. Breyer, *The Uneasy Case for Copyright*, 84 HARV. L. REV. 281, 322-323 (1970) (citing research in patent and copyright fields). Prometheus has offered no such

justification for its sweeping monopoly on medical thought and research.

Beyond this, the decision below cannot be reconciled with the ethical duties of physicians. As explained in amicus briefs filed in the Federal Circuit by the American Medical Association and other medical organizations, patent protection of Prometheus's claims conflicts with ethical standards that require physicians to spread knowledge—and improve diagnostic criteria—for the benefit of mankind.

The Federal Circuit's decision also poses exceptional threats to First Amendment freedoms. Throughout our Nation's history, the freedom to think—to consider what one has seen, to reach mental conclusions based on those observations, and to change one's future plans in light of those conclusions—has been deemed sacrosanct. Reflecting that tradition, this court held in *Ashcroft* v. *Free Speech Coalition*, 535 U.S. 234, 253 (2002), that speech is generally protected from government restriction because "[t]he right to think is the beginning of freedom, and speech must be protected from the government because speech is the beginning of thought." Federal legislation, like the patent laws, must be construed to avoid conflict with First Amendment freedoms whenever possible. See, *e.g.*, *New York* v. *Ferber*, 458 U.S. 747, 769 n.24 (1982); ACLU Am. Br. in *Bilski*, No. 2007-1130 (Fed. Cir. Apr. 3, 2008), at 5-7, 14, available at http://www.aclu.org/pdfs/freespeech/in_re_bilski_aclu_amicus.pdf (a patent like that at issue in *LabCorp* amounts "to a patent on pure thought or pure speech"; courts "should interpret patent law doctrines * * * so as to

avoid difficult application of First Amendment doctrines").

Yet the decision below would make mere thought actionable under patent law and threaten sanctions including actual and treble damages. 35 U.S.C. § 284. Simply drawing a mental conclusion becomes, under the Federal Circuit's view, patent infringement, even without any further act. The infringement is complete when a doctor has recognized a correlation between the patient's metabolite levels and the patient's status, regardless of what the doctor may do based on such recognition. This cannot be the legal rule in a Nation committed to the First Amendment and to the tradition of freedom of thought.

At bottom, the Federal Circuit's ruling authorizes patents over the mere observation of natural phenomena. That ruling flouts this Court's precedents and the fundamental purpose of the patent laws. And it puts a stranglehold on innovation and progress in the vital field of medical diagnosis.

CONCLUSION

The petition for a writ of certiorari should be granted to resolve the issues left undecided in *LabCorp*. At a minimum, the petition should be granted, the decision below vacated, and the case remanded for reconsideration in light of this Court's decision in *Bilski*.

Respectfully submitted.

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OCTOBER 2009

APPENDIX

APPENDIX A

UNITED STATES COURT OF APPEALS FOR THE FEDERAL CIRCUIT

2008-1403

PROMETHEUS LABORATORIES, INC.,
Plaintiff-Appellant,
v.
MAYO COLLABORATIVE SERVICES (doing business as Mayo Medical Laboratories) and MAYO CLINIC ROCHESTER,
Defendants-Appellees.

Appeal from the United States District Court for the Southern District of California in Case No. 04-CV-1200, Judge John A. Houston.

DECIDED: September 16, 2009

Before MICHEL, *Chief Judge*, LOURIE, *Circuit Judge*, and CLARK, District Judge.*

LOURIE, Circuit Judge.

Prometheus Laboratories, Inc. ("Prometheus") appeals from the final judgment of the United States District Court for the Southern District of California granting summary judgment of invalidity of U.S. Pa-

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* Honorable Ron Clark, District Judge, United States District Court for the Eastern District of Texas, sitting by designation.

tents 6,355,623 ("the '623 patent") and 6,680,302 ("the '302 patent") under 35 U.S.C. § 101. *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, No. 04-CV-1200, 2008 WL 878910 (S.D. Cal. Mar. 28, 2008) ("*Invalidity Opinion*"). Because the district court erred as a matter of law in finding the asserted claims to be drawn to non-statutory subject matter, we reverse.

I. BACKGROUND

Prometheus is the sole and exclusive licensee of the '623 patent and the '302 patent. The patents claim methods for calibrating the proper dosage of thiopurine drugs, which are used for treating both gastrointestinal and non-gastrointestinal autoimmune diseases. These drugs include 6-mercaptopurine ("6-MP") and azathiopurine ("AZA"), a pro-drug that upon administration to a patient converts to 6-MP, which are used to treat inflammatory bowel diseases ("IBD") such as Crohn's disease and ulcerative colitis. 6-MP is broken down by the body into various 6-MP metabolites, including 6-methyl-mercaptopurine ("6-MMP") and 6-thioguanine ("6-TG") and their nucleotides.[1] The patents involve measurements of these two metabolites. Drugs that deliver 6-TG are widely used for their cytotoxic and immunosuppressive properties.

Although drugs such as 6-MP and AZA have been used for years to treat autoimmune diseases, non-responsiveness and drug toxicity may complicate treatment in some patients. To that end, the patents claim methods that seek to optimize therapeutic efficacy while minimizing toxic side effects. As written,

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[1] For the purposes of this opinion, "6-TG" encompasses 6-thioguanine nucleotides.

the methods typically include two separately lettered steps: (a) "administering" a drug that provides 6-TG to a subject and (b) "determining" the levels of the drug's metabolites, 6-TG and/or 6-MMP, in the subject. *See, e.g.*, '623 patent claim 1. The measured metabolite levels are then compared to pre-determined metabolite levels, "wherein" the measured metabolite levels "indicate a need" to increase or decrease the level of drug to be administered so as to minimize toxicity and maximize efficacy of treatment. *See, e.g.*, *id.* In particular, according to the patents, a 6-TG level greater than about 400 picomole ("pmol") per 800 million red blood cells or a 6-MMP level greater than about 7000 pmol per 800 million red blood cells indicates that a downward adjustment in drug dosage may be required in order to avoid toxic side effects. *See id.* col.20 ll.22, 54. Conversely, according to the patents, a 6-TG level of less than about 230 pmol per 800 million red blood cells indicates a need to increase the dosage to ensure therapeutic efficacy. *See id.* col.20 ll.18-19.

Claim 1 of the '623 patent is representative of the independent claims asserted by Prometheus in this case:

> A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising:
>
> (a) administering a drug providing 6-thioguanine to a subject having said immune-mediated gastrointestinal disorder; and
>
> (b) determining the level of 6-thioguanine in said subject having said immune-mediated gastrointestinal disorder,

wherein the level of 6-thioguanine less than about 230 pmol per $8x10^8$ red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject and

wherein the level of 6-thioguanine greater than about 400 pmol per $8x10^8$ red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.

Claim 1 of the '302 patent is substantially the same, with the inclusion of determining 6-MMP levels in addition to 6-TG.

Prometheus marketed a PROMETHEUS Thiopurine Metabolites test (formerly known as the PRO-PredictRx® Metabolites test) that used the technology covered by the patents in suit. Mayo Collaborative Services and Mayo Clinic Rochester (together, "Mayo") formerly purchased and used Prometheus's test, but in 2004, Mayo announced that it intended to begin using internally at its clinics and selling to other hospitals its own test. Mayo's test measured the same metabolites as Prometheus's test, but Mayo's test used different levels to determine toxicity of 6-TG and 6-MMP.

On June 15, 2004, Prometheus sued Mayo for infringement of the patents. Prometheus asserted independent claims 1, 7, 22, 25, and 46 of the '623 patent and independent claim 1 of the '302 patent. Most of these claims cover a "method for optimizing therapeutic efficacy" and/or "reducing toxicity" in patients taking a drug such as AZA or 6-MP in the treatment of an immune-mediated gastrointestinal disease. *See* '623 patent claims 1, 7, 25, & 46; '302 patent claim 1. One independent claim was for

treatment of a non-IBD autoimmune disease. *See* '623 patent claim 22. Prometheus also asserted several dependent claims that require either that the measurement of the metabolites is done using high pressure liquid chromatography, *see* '623 patent claims 6, 14, 24, 30, and 53, or that the thiopurine drug used is one of four specified drugs, *see* '623 patent claims 32, 33, 35, and 36. Mayo rescinded its announcement shortly after the lawsuit was filed and still has not launched its test.

On November 22, 2005, the district court held on cross-motions for summary judgment that Mayo's test literally infringed claim 7 of the '623 patent. *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, No. 04-CV-1200, slip op. at 23 (S.D. Cal. Nov. 22, 2005) (Dkt. No. 227). In its opinion, the court construed "indicates a need" to mean "a warning that an adjustment in dosage may be required." *Id.* at 18. This construction did not require doctors to adjust drug dosage if the metabolite level reached the specified levels; rather, the court found the wherein phrases to mean "that when the identified metabolites reach the specified level, the doctor is warned or notified that a dosage adjustment may be required, if the doctor believes that is the proper procedure." *Id.* at 17-18.

On January 29, 2007, Mayo filed a motion for summary judgment of invalidity, arguing that the patents in suit are invalid because they claim unpatentable subject matter under 35 U.S.C. § 101. Specifically, Mayo contended that the patents impermissibly claim natural phenomena—the correlations between, on the one hand, thiopurine drug metabolite levels and, on the other hand, efficacy and toxici-

ty—and that the claims wholly preempt use of the natural phenomena.

On March 28, 2008, the district court granted Mayo's motion for summary judgment of invalidity under § 101. First, the court found that the patents claimed the correlations between certain thiopurine drug metabolite levels and therapeutic efficacy and toxicity. The court reasoned that, as construed in the November 2005 summary judgment order, the claims have three steps: (1) administer the drug to a subject; (2) determine metabolite levels; and (3) be warned that an adjustment in dosage may be required. The court stated that the fact that inventors framed the claims as treatment methods does not render the claims patentable. Rather, the court found that the "'administering' and 'determining' steps are merely necessary data-gathering steps for any use of the correlations" and that "as construed, the final step—the 'warning' step (i.e. the 'wherein' clause)—is only a mental step." *Invalidity Opinion*, 2008 WL 878910, at *6. The court noted that the warning step does not require any actual change in dosage and that "it is the metabolite levels themselves that 'warn' the doctor that an adjustment in dosage may be required." *Id.* With this understanding of the claims, the court concluded that the claims recited the correlations between particular concentrations of 6-TG and 6-MMP and therapeutic efficacy or toxicity in patients taking AZA drugs.

Second, the district court found that those correlations were natural phenomena and not patentable inventions because the correlations resulted from a natural body process. The court stated that the inventors did not "invent" the claimed correlation; rather, "6-TG and 6-MMP are products of the natural

metabolizing of thiopurine drugs, and the inventors merely observed the relationship between these naturally produced metabolites and therapeutic efficacy and toxicity." *Invalidity Opinion*, 2008 WL 878910, at *7. Finally, the court determined that "[b]ecause the claims cover the correlations themselves, it follows that the claims 'wholly pre-empt' the correlations." *Id.* at *11. Thus, the court concluded that there was no genuine issue of material fact to be resolved as to whether the patents in suit were directed to statutory subject matter and found by clear and convincing evidence that the claims were invalid under § 101.

On May 16, 2008, the district court entered final judgment, disposing of all the parties' claims and counterclaims. On May 30, 2008, Prometheus timely appealed the district court's grant of summary judgment of invalidity under § 101. We have jurisdiction pursuant to 28 U.S.C. § 1295(a)(1).

II. DISCUSSION

A. Standard of Review

We review the district court's grant of summary judgment *de novo*. *AT&T Corp. v. Excel Commc'ns*, 172 F.3d 1352, 1355 (Fed. Cir. 1999). Summary judgment is appropriate if there are no genuine issues of material fact and the moving party is entitled to judgment as a matter of law. *Id.*; Fed. R. Civ. P. 56(c). Whether a patent claim is directed to statutory subject matter is a question of law that we review *de novo*. *AT&T*, 172 F.3d at 1355.

B. Section 101

The issue before us is whether the claims meet the requirements of § 101, so we begin with the text of the statute. Section 101 provides that:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent thereof, subject to the conditions and requirements of this title.

35 U.S.C. § 101. According to § 100(b), "[t]he term 'process' means process, art, or method, and includes a new use of a known process, machine, manufacture, composition of matter, or materials." 35 U.S.C. § 100(b). But, as noted in *In re Bilski*, this definition of process is "unhelpful" because the definition itself uses the term "process." 545 F.3d 943, 951 n.3 (Fed. Cir. 2008) (en banc), *cert. granted*, 129 S. Ct. 2735 (June 1, 2009). Thus, we turn to the case law to guide our understanding of what constitutes statutory subject matter under § 101.

The Supreme Court has construed § 101 broadly, noting that Congress intended statutory subject matter to "include anything under the sun that is made by man." *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980). It is well-established, however, that this sweeping statement does not indicate that § 101 is unlimited and embraces every discovery:

> [A] new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter. Likewise, Einstein could not patent his celebrated law that $E=mc^2$; nor could Newton have patented the law of gravity. Such discoveries are "manifestations of . . . nature, free to all men and reserved exclusively to none."

Id. (quoting *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948)). More specifically, the Court has held that a claim to a process is not patent-eligible if it claims "laws of nature, natural phe-

nomena, and abstract ideas." *Diamond v. Diehr*, 450 U.S. 175, 185 (1981); *see also Gottschalk v. Benson*, 409 U.S. 63, 67 (1972) ("Phenomena of nature, though just discovered, mental processes, and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work.").

At the same time, it has also been established that "while a claim drawn to a fundamental principle"—*i.e.*, a law of nature, natural phenomenon, or abstract idea—"is unpatentable, 'an *application* of a law of nature or mathematical formula to a known structure or process may well be deserving of patent protection.'" *Bilski*, 545 F.3d at 953 (quoting *Diehr*, 450 U.S. at 187). The key issue for patentability, then, at least on the present facts, is whether a claim is drawn to a fundamental principle or an application of a fundamental principle. Although this inquiry is hardly straightforward, following the Supreme Court, we articulated in *Bilski* a "definitive test" for determining whether a process is patent-eligible under § 101: "A claimed process is surely patent-eligible under § 101 if: (1) it is tied to a particular machine or apparatus, or (2) it transforms a particular article into a different state or thing." *Id.* The machine-or-transformation test is a "two-branched inquiry," *i.e.*, the patentee "may show that a process claim satisfies § 101 either by showing that his claim is tied to a particular machine, or by showing that his claim transforms an article." *Id.* at 961.

The machine-or-transformation test has two further aspects: "the use of a specific machine or transformation of an article must impose meaningful limits on the claim's scope to impart patent-eligibility," and "the involvement of the machine or

transformation in the claimed process must not merely be insignificant extra-solution activity." *Bilski*, 545 F.3d at 961-62 (citations omitted). "This transformation must be central to the purpose of the claimed process." *Id.* at 962. Thus, in most cases, one cannot ground the transformative nature of a process in a step that is "insignificant extra-solution activity" or merely a "data-gathering step." *See id.* at 963 ("Further, the inherent step of gathering data can also fairly be characterized as insignificant extra-solution activity."). In other words, if steps of a method are included for the purpose of data-gathering rather than being "central" to the purpose of the process, the patentee likely cannot rely on the data-gathering steps to prove that the claimed process is transformative and thus drawn to patentable subject matter. *See id.* at 963 (stating that mere data-gathering will not, "at least in most cases, . . . constitute a transformation of any article").

The Supreme Court has also made clear that the patent eligibility of a claim as a whole should not be based on whether selected limitations constitute patent-eligible subject matter. *See Bilski*, 545 F.3d at 958 (citing *Diehr*, 450 U.S. at 188; *Parker v. Flook*, 437 U.S. 584, 594 (1978)). As noted in *Diehr*, the Court has specifically stated that it is "inappropriate to dissect the claims into old and new elements and then to ignore the presence of the old elements in the analysis." 450 U.S. at 188. Moreover, it is improper to consider whether a claimed element or step in a process is novel or nonobvious, since such considerations are separate requirements set forth in 35 U.S.C. §§ 102 and 103, respectively. *Bilski*, 545 F.3d at 958 (citing *Diehr*, 450 U.S. at 188-91). With this understanding of the present state of the law, we

now turn to the parties' arguments in the instant action.

C. Analysis

On appeal, Prometheus argues that the claimed processes satisfy § 101 because they meet both prongs of the machine-or-transformation test articulated in *Bilski*. With respect to the machine prong, Prometheus argues that the patents inextricably rely on numerous machines to process the bodily sample, determine the metabolite levels, and thereby calibrate the proper dose. Prometheus asserts that the district court erred by failing to consider separately the asserted dependent claims, some of which specify measurement through high pressure liquid chromatography, which clearly requires the use of machines. In addition, Prometheus contends that *Bilski*'s use of "machine" in its machine-or-transformation test must be read as shorthand for all patentable subject matter, including compositions of matter. To that end, Prometheus argues that the synthetic drugs used in its treatment methods are compositions of matter, and the claims' central reliance on those drugs is enough to meet the machine-or-transformation test. Alternatively, Prometheus asserts that we should recognize that *Bilski* does not apply where, as here, the treatment methods use synthetic drugs and thus do not recite or wholly preempt any natural phenomenon.

With respect to the transformation prong, Prometheus points to three "transformations" within its claimed process: (1) the first step of administering a synthetic drug transforms the biochemical makeup of the patient's body for the purpose of treating disease; (2) the second step requires the transformation of a bodily sample to determine the created metabo-

lites' concentration levels; and (3) the metabolite levels are transformed into a warning for a doctor to alter the dosage. Regarding the first asserted transformation, Prometheus argues that physical transformations, such as the human body's metabolic reaction to drugs, initiated by human actions and artificial chemical compounds, such as the administration of a thiopurine drug into the body, cannot be unpatentable under *Bilski* simply because they proceed according to natural laws or occur within the human body. Prometheus contends that *everything* proceeds according to natural laws. Regarding the second asserted transformation, Prometheus argues that all of the several methods available to determine the metabolite levels in a bodily sample require a physical transformation of blood or human tissue in order to extract the metabolite and determine its concentration. Finally, regarding the third asserted transformation, Prometheus posits that the ultimate end of the processes is to transform—and improve—the patient's treatment regime while avoiding deadly side effects by transforming the metabolite levels into a warning regarding dosage.

Prometheus then argues that these machines and transformations are central to the invention's purpose of improving a process of treatment and are not confined to extra-solution activity. Prometheus asserts that the district court erred by parsing the steps of the treatment method rather than looking at the method as a whole, which applies the correlations in concrete physical processes—that Prometheus argues are patentable absent the correlation—to generate useful information. Prometheus contends that adoption of the district court's reasoning would have the effect of eliminating all medical treatment

and diagnostic patents, when future medical advances will depend on optimizing treatment based on genetic or other testing.

Mayo responds that the district court properly examined the claims as a whole and correctly determined that they recite the correlations themselves, which are natural phenomena. With respect to the machine prong, Mayo argues that any involvement of machines is insignificant extra-solution activity. Mayo asserts that the step of determining the metabolite levels via an unspecified machine is merely gathering data that is necessary to correlate information. Mayo argues that *Bilski* requires the use of a "particular machine or apparatus" and that no particular machine is involved in Prometheus's process. Mayo contends that Prometheus's reliance on the dependent claims reciting the use of high pressure liquid chromatography is misplaced because choosing to limit the claims to one possible method for performing one of the steps is not sufficient to impart patentability over a natural phenomenon.

Similarly, with respect to the transformation prong, Mayo argues that there is no patentable transformation in the claimed processes. First, Mayo asserts that the administering step is merely a data-gathering step. Mayo points out that the asserted claims do not all include the administering step and thus argues that the administration of the drug cannot be central to the claim. Mayo also contends that although the thiopurine drugs used in the claims are synthetic, the body's reaction to them is natural, and the drugs themselves were well known. Second, Mayo argues that the determining step is also data-gathering necessary to make any use of the correlations, and the presence of the physical step of trans-

forming clinical samples does not impart patentability to claims to natural correlations. Third, Mayo argues that there is no transformation of data into a warning because the claims do not require any action to be taken to adjust dosage. Under the claim construction argued by Prometheus and adopted by the district court, the final step is a mental step and thus, Mayo argues, the data undergoes no transformation at all.

Furthermore, Mayo asserts that the district court properly determined not only that the claims were to the correlations themselves but that the claims preempt all practical use of the correlations. Post-*Bilski*, Mayo argues that Supreme Court precedent invalidating a claim that wholly preempts a natural phenomenon such that the practical effect is a patent on the phenomenon itself still stands. Mayo contends that because nothing is done with the naturally occurring correlation, the claims cover all implementations resulting from that natural phenomenon and are thus unpatentable. Finally, Mayo argues that invalidating Prometheus's claims will not affect medical treatment methods because infringement of the asserted claims requires no act by a physician at all and no treatment of any disease or condition in a patient. Furthermore, Mayo asserts that upholding the claims under § 101 is dangerous because infringement would occur any time the natural correlation was even considered by a physician.

A number of amici curiae filed helpful briefs on both sides. Those supporting Prometheus argued that the transformation that flows from the use of thiopurine drugs in the patented processes is not "insignificant" post-solution activity but rather a specific and practical application of the correlations in

medical treatment. They also argue that the future of personalized medicine will involve knowledge of the physiological or biological significance of biomarkers and how to use them in diagnostic or therapeutic procedures and that patents on those biomarkers should be granted. Those supporting Mayo argue that the district court properly found that the claims impermissibly preempt a natural statistical correlation by asserting exclusive rights over the mere recognition by a treating physician of those correlations. They argue that finding Prometheus's claim to cover patentable subject matter would be granting exclusive rights over mere knowledge of the correlations and would thus interfere with the provision of medical care and with research and quality control in clinical chemistry.

1. *The administering and determining steps are transformative*

We agree with Prometheus that the asserted claims are drawn to statutory subject matter and thus reverse the district court's grant of Mayo's motion for summary judgment of invalidity. As an initial matter, we note that the only issue before us is whether the claims meet the requirements of § 101. This appeal does not raise any questions about lack of novelty, obviousness, or overbreadth, since those are separate statutory requirements for patentability under §§ 102, 103, and 112, respectively. *See Bilski*, 545 F.3d at 958 (citing *Diehr*, 450 U.S. at 188-91). The proper inquiry under § 101 is whether these methods meet the Supreme Court's machine or transformation test articulated in *Benson* and *Diehr*, and applied in *Bilski*, and, if so, whether the machine or

the transformation is central to the purpose of the claims.[2]

We conclude that the methods of treatment claimed in the patents in suit squarely fall within the realm of patentable subject matter because they "transform an article into a different state or thing," and this transformation is "central to the purpose of the claimed process." *See Bilski*, 545 F.3d at 962. The transformation is of the human body following administration of a drug and the various chemical and physical changes of the drug's metabolites that enable their concentrations to be determined. Because the claimed methods meet the transformation prong under *Bilski*, we do not consider whether they also meet the machine prong.

Contrary to the district court, we do not view the disputed claims as merely claiming natural correlations and data-gathering steps.[3] The asserted claims are in effect claims to methods of treatment,

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[2] We note that the district court did not have the benefit of our *Bilski* decision when deciding the § 101 issue. However, we believe that even prior to *Bilski*, the asserted claims should have been found to be patentable subject matter under the Supreme Court's decisions in *Benson* and *Diehr* and our cases such as *In re Grams*, 888 F.2d 835 (Fed. Cir. 1989), and *In re Abele*, 684 F.2d 902 (CCPA 1982).

[3] In reaching its conclusion, the district court relied heavily on the opinion of three justices dissenting from the dismissal of the grant of certiorari in *Laboratory Corp. of America Holdings v. Metabolite Laboratories, Inc.*, 548 U.S. 124 (2006) (Breyer, J., dissenting). *See Invalidity Opinion*, 2008 WL 878910, at *8 (discussing the dissent in *Laboratory Corp.* at length and stating that although the dissent "does not have precedential value, the Court finds Justice Breyer's reasoning persuasive"). That dissent is not controlling law and also involved different claims from the ones at issue here.

which are always transformative when a defined group of drugs is administered to the body to ameliorate the effects of an undesired condition. More specifically, Prometheus here claimed methods for optimizing efficacy and reducing toxicity of treatment regimes for gastrointestinal and non-gastrointestinal autoimmune diseases that utilize drugs providing 6-TG by administering a drug to a subject. The invention's purpose to treat the human body is made clear in the specification and the preambles of the asserted claims. *See* '623 patent col.2 ll.16-19 ("The present invention provides a method of optimizing therapeutic efficacy of 6-mercaptopurine drug treatment of an immune-mediated gastrointestinal disorder."); *see, e.g.*, *id.* claim 1 ("A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising . . ."); *id.* claim 7 ("A method of reducing toxicity associated with treatment of an immune-mediated gastrointestinal disorder, comprising . . ."); *id.* claim 22 ("A method of optimizing therapeutic efficacy of treatment of a non-IBD autoimmune disease, comprising . . .").

When administering a drug such as AZA or 6-MP, the human body necessarily undergoes a transformation. The drugs do not pass through the body untouched without affecting it. In fact, the transformation that occurs, *viz.*, the effect on the body after metabolizing the artificially administered drugs, is the entire purpose of administering these drugs: the drugs are administered to provide 6-TG, which is thought to be the drugs' active metabolite in the treatment of disease, to a subject. *See* '623 patent col.1 ll.49-51. The fact that the change of the administered drug into its metabolites relies on natural processes does not disqualify the administering step

from the realm of patentability. As Prometheus points out, quite literally every transformation of physical matter can be described as occurring according to natural processes and natural law. Transformations operate by natural principles. The transformation here, however, is the result of the physical administration of a drug to a subject to transform—*i.e.*, treat—the subject, which is itself not a natural process. "It is virtually self-evident that a process for a chemical or physical transformation of *physical objects or substances* is patent-eligible subject matter." *See Bilski*, 545 F.3d at 962. The administering step, therefore, is not merely data-gathering but a significant transformative element of Prometheus's claimed methods of treatment that is "sufficiently definite to confine the patent monopoly within rather definite bounds." *Id.* (quoting *Benson*, 409 U.S. at 70).

Mayo is correct that not all of the asserted claims contain the administering step. That omission, which occurs in claims 46 and 53 of the '623 patent, does not diminish the patentability of the claimed methods because the determining step, which is present in each of the asserted claims, is also transformative and central to the claimed methods. Determining the levels of 6-TG or 6-MMP in a subject necessarily involves a transformation, for those levels cannot be determined by mere inspection. Some form of manipulation, such as the high pressure liquid chromatography method specified in several of the asserted dependent claims or other modification of the substances to be measured, is necessary to extract the metabolites from a bodily sample and determine their concentration. As stated by Prometheus's expert, "at the end of the process, the human blood sample is no longer human blood; hu-

man tissue is no longer human tissue." Decl. of Dr. Yves Théorêt ¶ 6, *Prometheus Labs., Inc. v. Mayo Collaborative Servs.*, No. 04-CV-1200 (S.D. Cal. Mar. 29, 2007) (Dkt. No. 528-3). That is clearly a transformation. In fact, Mayo does not dispute that determining metabolite levels in the clinical samples taken from patients is transformative, but argues that this transformation is merely a necessary data-gathering step for use of the correlations. Appellees' Br. 37 ("The 'transformation' of the patient's sample is merely a necessary data-gathering step. . . . [T]he presence of the physical step of transforming clinical samples taken from patients does not impart patentability to Prometheus' claims to the natural correlations."). On the contrary, this transformation is central to the purpose of the claims, since the determining step is, like the administering step, a significant part of the claimed method of treatment. Measuring the levels of 6-TG and 6-MMP is what enables possible adjustments to thiopurine drug dosage to be detected for optimizing efficacy or reducing toxicity during a course of treatment. The determining step, by working a chemical and physical transformation on physical substances, likewise sufficiently confines the patent monopoly, as required by *Bilski*.

2. *The administering and determining steps are not merely data-gathering*

A further requirement for patent-eligibility is ensuring that the involvement of the transformation in Prometheus's claimed process is "not merely insignificant extra-solution activity." *Bilski*, 545 F.3d at 962 (citing *Flook*, 437 U.S. at 590). As made clear from the discussion above, the administering and determining steps are transformative and are central

to the claims rather than merely insignificant extra-solution activity.

The crucial error the district court made in reaching the opposite conclusion was failing to recognize that the first two steps of the asserted claims are not merely data-gathering steps. *See Invalidity Opinion*, 2008 WL 878910, at *6 (finding that "the 'administering' and 'determining' steps are merely necessary data-gathering steps for any use of the correlations"). While it is true that the administering and determining steps gather useful data, it is also clear that the presence of those two steps in the claimed processes is not "merely" for the purpose of gathering data. Instead, the administering and determining steps are part of a treatment protocol, and they are transformative. As explained above, the administering step provides thiopurine drugs for the purpose of treating disease, and the determining step measures the drugs' metabolite levels for the purpose of assessing the drugs' dosage during the course of treatment.

Given the integral involvement of the administering and determining steps in Prometheus's therapeutic methods, this case is easily distinguishable from prior cases that found asserted method claims to be unpatentable for claiming data-gathering steps and a fundamental principle. Perhaps the case that offers the closest comparison is *In re Grams*, 888 F.2d 835 (Fed. Cir. 1989), but the asserted claims found unpatentable in that case are readily distinguished from those in the instant action. In *Grams*, the applicant claimed a process that involved (1) performing a clinical test on individuals and (2) based on the data from that test, determining if an abnormality existed and determining possible

causes of any abnormality by using an algorithm. We found that this process was not drawn to patentable subject matter because the essence of the claimed process was the mathematical algorithm, rather than any transformation of the tested individuals. 888 F.2d at 839-41. More specifically, the *Grams* process was unpatentable because "it was merely an algorithm combined with a data-gathering step," *i.e.*, performing a clinical test. *Bilski*, 545 F.3d at 963. The claims did not require the performing of clinical tests on individuals that were transformative—and thus rendering the entire process patentable subject matter—because the tests were just to "obtain data." *Grams*, 888 F.2d at 840. The patent and thus the court focused only on the algorithm rather than the clinical tests purported to be covered by the claims.

Here, unlike the clinical test recited in *Grams*, the administering and determining steps in Prometheus's claimed methods are not "merely" data-gathering steps or "insignificant extra-solution activity"; they are part of treatment regimes for various diseases using thiopurine drugs. *See Bilski*, 545 F.3d at 963 (discussing *Grams*). As a result, the administering and determining steps are not insignificant extra-solution activity, and the claims are therefore not drawn merely to correlations between metabolite levels and toxicity or efficacy.

3. *The presence of a mental step does not detract from patentability*

We agree with the district court that the final "wherein" clauses are mental steps and thus not patent-eligible per se. However, although they alone are not patent-eligible, the claims are not simply to the mental steps. A subsequent mental step does not, by itself, negate the transformative nature of prior

steps. Thus, when viewed in the proper context, the final step of providing a warning based on the results of the prior steps does not detract from the patentability of Prometheus's claimed methods as a whole. The data that the administering and determining steps provide for use in the mental steps is obtained by steps well within the realm of patentable subject matter. The addition of the mental steps to the claimed methods thus does not remove the prior two steps from that realm.

This analysis is consistent with *In re Abele*, 684 F.2d 902 (CCPA 1982).[4] In *Abele*, a method claim called for the use of X-ray attenuation data, which necessarily involved production, detection, and display with a CAT scan. The method also called for use of an algorithm. We found that the claim was patentable because removal of the algorithm still left all the steps of a CAT scan in the claim; thus, the production and detection could not be considered "mere antecedent steps to obtain values for solving the algorithm. . . . We view the production, detection, and display steps as manifestly statutory subject matter, and are not swayed from this conclusion by the presence of an algorithm in the claimed method." *Id.* at 908. In the instant case, the presence of the mental steps similarly does not detract from the patentability of the administering and determining steps.

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[4] Although *Bilski* reiterated that the *Freeman-Walter-Abele* test is "inadequate" for determining patent-eligibility, *Bilski* spoke approvingly of the analysis regarding the patent-eligible method in *Abele*. *See Bilski*, 545 F.3d at 962-63. Thus, the determination that claim 6 of Abele's patent was patent-eligible subject matter is still good law post-*Bilski*.

As we explained in *Bilski*,

> [I]t is inappropriate to determine the patent eligibility of a claim as a whole based on whether selected limitations constitute patent-eligible subject matter. After all, even though a fundamental principle itself is not patent-eligible, processes incorporating a fundamental principle may be patent-eligible. Thus, it is irrelevant that any individual step or limitation of such processes by itself would be unpatentable under § 101.

545 F.3d at 958 (citations omitted). Such is the case here. Although the wherein clauses describe the mental processes used to determine the need to change the dosage levels of the drugs, each asserted claim as a whole is drawn to patentable subject matter. Although a physician is not required to make any upward or downward adjustment in dosage during the "warning" step, the prior steps provide useful information for possible dosage adjustments to the method of treatment using thiopurine drugs for a particular subject. When viewing the treatment methods as a whole, Prometheus has claimed therapeutic methods that determine the optimal dosage level for a course of treatment. In other words, when asked the critical question of "What did the applicant invent?," *Grams*, 888 F.2d at 839 (citation omitted), the answer is a series of transformative steps that optimizes efficacy and reduces toxicity of a method of treatment for particular diseases using particular drugs.

Furthermore, the district court erred in finding that the claims wholly preempt use of correlations between metabolite levels and efficacy or toxicity. The court reached this conclusion because "the

claims cover the correlations themselves." *Invalidity Opinion*, 2008 WL 878910, at *11. As discussed above, the claims are to transformative methods of treatment, not correlations. The claims cover a particular application of natural processes to treat various diseases, but transformative steps utilizing natural processes are not unpatentable subject matter. Moreover, the claims do not preempt natural processes; they utilize them in a series of specific steps. *See Diehr*, 450 U.S. at 187 ("Their process admittedly employs a well-known mathematical equation, but they do not seek to preempt the use of that equation. Rather, they seek only to foreclose from others the use of that equation in conjunction with all of the other steps in their claimed process."). Regardless, because the claims meet the machine-or-transformation test, they do not preempt a fundamental principle. *See Bilski*, 545 F.3d at 954 (characterizing the machine-or-transformation test as "a definitive test to determine whether a process is tailored narrowly enough to encompass only a particular application of a fundamental principle rather than to pre-empt the principle itself"). The inventive nature of the claimed methods stems not from preemption of all use of these natural processes, but from the application of a natural phenomenon in a series of transformative steps comprising particular methods of treatment. *See id.* ("[A] claimed process that transforms a particular article to a specified different state or thing by applying a fundamental principle would not pre-empt the use of the principle to transform any other article, to transform the same article but in a manner not covered by the claim, or to do anything other than transform the specified ar-

ticle."). It is clear that these methods of treatment are § 101 patentable subject matter.

Thus, the claimed methods satisfy all of the requirements under *Bilski*'s transformation prong for patent-eligible subject matter under § 101.

III. CONCLUSION

For the foregoing reasons, we reverse the judgment of the district court and remand to the court with instructions to deny Mayo's motion for summary judgment that the asserted claims are invalid under § 101.

REVERSED and *REMANDED*

APPENDIX B

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF CALIFORNIA

Civil No. 04cv1200 JAH (RBB)

PROMETHEUS LABORATORIES, INC.,
Plaintiff,

v.

MAYO COLLABORATIVE SERVICES dba MAYO MEDICAL LABORATORIES AND MAYO CLINIC ROCHESTER,
Defendants

AND RELATED COUNTERCLAIM.

ORDER

1. GRANTING DEFENDANTS' MOTION FOR SUMMARY JUDGMENT OF PATENT INVALIDITY PURSUANT TO 35 U.S.C. § 101 [Doc. No. 502];

2. DENYING AS MOOT PLAINTIFF'S MOTION FOR SUMMARY JUDGMENT OF NO PATENT EXHAUSTION [Doc. No. 494];

3. DENYING AS MOOT PLAINTIFF'S MOTION FOR SUMMARY JUDGMENT OF DECLARATORY INFRINGEMENT OF PATENT NOS. 6,355,623 AND 6,680,302 [Doc. No. 439];

4. DENYING AS MOOT PLAINTIFF'S MOTION TO STRIKE DECLARATION OF DR. BRUCE BOSTROM [Doc. No. 549]

INTRODUCTION

Now before the Court are three motions for summary judgment filed by the parties, and a motion to strike the declaration of Dr. Bruce Bostrom filed by Plaintiff. The motions have each been fully briefed and oral argument has been entertained. After careful consideration of the pleadings and relevant exhibits presented by the parties, the oral argument presented at the hearing, and for the reasons set forth below, this Court **GRANTS** Defendants' motion for summary judgment of patent invalidity thereby invalidating the patents-in-suit as violative of 35 U.S.C. § 101. Accordingly, Plaintiff's motions for summary judgment of no patent exhaustion and for declaratory judgment of infringement are **DENIED as moot**, and will not be addressed herein. Plaintiff's motion to strike the declaration of Dr. Bruce Bostrom is also **DENIED as moot.**

BACKGROUND

A. Factual Background

Plaintiff, Prometheus Laboratories ("Plaintiff" or "Prometheus"), is the exclusive licensee of two patents: U.S. Patent Nos. 6,355,623 ("the '623 patent") and 6,680,302 ("the '302 patent") (collectively "the patents-in-suit"). The patents-in-suit involve measurements of the level of certain metabolites in the blood of patients taking thiopurine drugs, including the anti-Crohn's disease drug azathioprine ("AZA"), for treatment of either gastrointestinal autoimmune diseases or non-gastrointestinal autoimmune diseases. The patented test provides a means to measure the level of two metabolites: 6-thioguinine ("6-TG") and 6-methylmercaptopurine ("6-MMP"), which, ac-

cording to the patent, indicates that an adjustment in drug dosage may be required at metabolite levels "greater than about 400" and "greater than about 7000," respectively, in order to avoid toxic side effects.

Defendants, Mayo Collaborative Services dba Mayo Medical Laboratories and Mayo Clinic Rochester (collectively "Defendants" or "Mayo") developed a test ("the accused test") to measure the same metabolites but using different levels, 450 6-TG and 5700 6-MMP. In June 2004, Defendants announced they intended to begin use of their accused test, offering it for sale to potential purchasers, but the announcement was later rescinded. The instant lawsuit followed.

B. Procedural History

Plaintiff filed its patent infringement complaint on June 15, 2004. On January 27, 2005, Defendants filed a motion for summary judgment seeking a declaration of non-infringement, which this Court denied on November 22, 2005. Doc. No. 227. Plaintiff filed a cross-motion for summary judgment, seeking a judicial declaration that Defendants' accused test literally infringes Claim 7 of the '623 patent, which this Court granted in its November 22, 2005 order.[1] Defendants filed a motion seeking relief

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[1] In its November 22, 2005 order, this Court construed the following terms contained in the patents-in-suit: (1) "greater than about 400" was construed to mean "any level above 340 to 460"; and "indicates a need" was construed to mean "a warning that an adjustment in dosage may be required." Doc. No. 227 at 18.

from the Court's November 22, 2005 order, which the Court denied. Doc. Nos. 230 and 260.

On December 13, 2005, this Court granted both parties' motions to amend their respective pleadings. Doc. No. 234. Plaintiff filed a first amended complaint ("FAC") on December 22, 2005. Doc. No. 236. Defendants filed an answer to the FAC, along with amended counterclaims, on January 13, 2006. Doc. No. 241. On April 14, 2006, the parties stipulated to the filing of a second amended complaint ("SAC"). Doc. No. 267.

Three separate motions for summary judgment followed. On January 9, 2007, Plaintiff filed a motion for summary judgment of no patent exhaustion. Doc. No. 494. Defendants filed an opposition to Plaintiff's motion on February 22, 2007. Doc. No. 519. Plaintiff filed a reply on March 1, 2007. Doc. No. 529.

Defendants filed a motion for summary judgment of patent invalidity under 35 U.S.C. § 101 on January 29, 2007.[2] Doc. No. 502. Plaintiff filed an opposition to Defendants' motion on February 28, 2007. Doc. No. 528. Defendants filed their reply on March 9, 2007. Doc. No. 542. Included in Defendants' reply brief was a declaration by Dr. Bruce Bostrom. Plaintiff subsequently filed a motion to strike Dr. Bostrom's declaration. Doc. No. 549. Defendants filed

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[2] Defendants also filed, on January 25, 2007, a motion to strike Plaintiff's jury demand. Doc. No. 501. Because Plaintiff did not oppose the motion, the Court subsequently granted the motion and struck the jury demand. Doc. No. 546.

an opposition to Plaintiff's motion and Plaintiff filed a reply. Doc. Nos. 566 and 568.

On March 8, 2007, Plaintiff filed a motion for summary judgment of declaratory judgment of infringement. Doc. No. 539. Defendants filed an opposition to Plaintiff's motion on April 12, 2007. Doc. No. 561. Plaintiff filed a reply on April 19, 2007. Doc. No. 565.

The Court rescheduled the motion hearing on the first summary judgment motions so that all motions (including the motion to strike the declaration of Bruce Bostrom) could be heard on the same day, May10, 2007, and set a briefing schedule for the remaining pleadings. On May 10, 2007, after all the motions were fully briefed, this Court heard oral argument from the parties and took all four motions under submission.

On October 1, 2007, while the motions were still under submission, the parties filed a joint application requesting permission to submit additional briefing on two recently decided Federal Circuit cases: *In re Comiskey*, 499 F.3d 1365 (Fed. Cir. 2007), and *In re Nuijten*, 500 F.3d 1346 (Fed. Cir. 2007). Doc. No. 584. The Court granted the request, and on October 26, 2007, Defendants submitted a brief regarding *Comiskey* and *Nuijten*. Doc. No. 586. Plaintiff submitted its own brief on November 9, 2007. Doc. No. 588. Defendants then requested, and were granted, leave to file a reply brief, which they filed on November 19, 2007. Doc. No. 590, Exhibit A. Plaintiff then submitted a sur-reply brief on November 30, 2007. Doc. No. 593.

DISCUSSION

Defendants have moved for summary judgment on the grounds that the patents-in-suit are invalid because they impermissibly claim unpatentable subject matter under 35 U.S.C. § 101. Specifically, Defendants contend that the patents impermissibly claim natural phenomena – the correlations between thiopurine drug metabolite levels on the one hand and therapeutic efficacy and toxicity on the other – and the claims "wholly pre-empt" use of the natural phenomena. *See* Doc. No. 502 at 11-12.

A. Legal Standards

1. Summary Judgment

Summary judgment is appropriate under Rule 56(c) of the Federal Rules of Civil Procedure where the moving party demonstrates the absence of a genuine issue of material fact and entitlement to judgment as a matter of law. Fed. R. Civ. P. 56(c); *Celotex Corp. v. Catrett*, 477 U.S. 317, 322 (1986). A fact is material when, under the governing substantive law, it could affect the outcome of the case. *See Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 248 (1986); *Freeman v. Arpaio*, 125 F.3d 732, 735 (9th Cir. 1997). A dispute about a material fact is genuine if "the evidence is such that a reasonable jury could return a verdict for the nonmoving party." *Anderson*, 477 U.S. at 248.

A party seeking summary judgment always bears the initial burden of establishing the absence of a genuine issue of material fact. *See Celotex*, 477 U.S. at 323. The moving party may satisfy this burden in two ways: (1) by presenting evidence that negates an essential element of the nonmoving party's

case or (2) by demonstrating that the nonmoving party failed to make a showing sufficient to establish an element essential to that party's case on which that party will bear the burden of proof at trial. *Id.* at 322-23. "Disputes over irrelevant or unnecessary facts will not preclude a grant of summary judgment." *T.W. Elec. Serv., Inc. v. Pacific Elec. Contractors Ass'n*, 809 F.2d 626, 630 (9th Cir. 1987). "The district court may limit its review to the documents submitted for purpose of summary judgment and those parts of the record specifically referenced therein." *Carmen v. San Francisco Unified Sch. Dist.*, 237 F.3d 1026, 1030 (9th Cir. 2001). Therefore, the court is not obligated "to scour the record in search of a genuine issue of triable fact." *Keenan v. Allen*, 91 F.3d 1275, 1279 (9th Cir. 1996) (citing *Richards v. Combined Ins. Co.*, 55 F.3d 247, 251 (7th Cir. 1995)). If the moving party fails to discharge this initial burden, summary judgment must be denied and the court need not consider the nonmoving party's evidence. *See Adickes v. S.H. Kress & Co.*, 398 U.S. 144, 159-60 (1970).

If the moving party meets the initial burden, the nonmoving party cannot defeat summary judgment merely by demonstrating "that there is some metaphysical doubt as to the material facts." *Matsushita Elec. Indus. Co., Ltd. v. Zenith Radio Corp.*, 475 U.S. 574, 586 (1986); *see also Anderson*, 477 U.S. at 252 ("The mere existence of a scintilla of evidence in support of the nonmoving party's position is not sufficient."). Rather, the nonmoving party must "go beyond the pleadings and by her own affidavits, or by the depositions, answers to interrogatories, and admissions on file, designate specific facts showing that there is a genuine issue for trial." *Celotex*, 477 U.S.

at 324 (quoting Fed. R. Civ. P. 56(e)) (internal quotations omitted).

When ruling on summary judgment, the court may not make credibility determinations, and inferences to be drawn from the facts must be viewed in the light most favorable to the party opposing the motion. *Masson v. New Yorker Magazine*, 501 U.S. 496 (1991); *see also Anderson*, 477 U.S. at 249, *Matsushita*, 475 U.S. at 587.

2. Section 101

Defendants move for summary judgment for patent invalidity under 35 U.S.C. § 101. Section 101 provides that:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.[3]

35 U.S.C. § 101

The Supreme Court has construed section 101 broadly, observing that Congress intended statutory subject matter to include "anything under the sun that is made by man." *Diamond v. Chakrabarty*, 447 U.S. 303, 309 (1980). However, it is well settled that there are qualifications to the apparent sweep of this

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[3] The word "process" is defined in 35 U.S.C. § 100(b): "The term 'process' means process, art, or method, and includes a new use of a known process, machine, manufacture, composition of matter, or material."

statement. In *Chakrabarty*, the Supreme Court explained that:

> [A] new mineral discovered in the earth or a new plant found in the wild is not patentable subject matter. Likewise, Einstein could not patent his celebrated law that $E = mc^2$; nor could Newton have patented the law of gravity. Such discoveries are 'manifestations of . . . nature, free to all men and reserved exclusively to none.'

447 U.S. at 309 (quoting *Funk Bros. Seed Co. v. Kalo Inoculant Co.*, 333 U.S. 127, 130 (1948)). Accordingly, the Supreme Court has specifically excluded from patentable subject matter: "laws of nature, natural phenomena, and abstract ideas." *Diamond v. Diehr*, 450 U.S. 175, 185 (1981). As the Court explained, "[p]henomena of nature, though just discovered, mental processes and abstract intellectual concepts are not patentable, as they are the basic tools of scientific and technological work." *Gottschalk v. Benson*, 409 U.S. 63, 67 (1972).

In assessing patentability under section 101 in the context of method patents, the Supreme Court has explained that a method patent is not invalid "simply because it contains a law of nature or a mathematical algorithm." *Parker v. Flook*, 437 U.S. 584, 590 (1978). But, if the claim "recites" a law of nature or a mathematical algorithm, the court must analyze whether the claim is seeking patent protection for the phenomenon "in the abstract" or whether the claim implements a natural phenomenon "in a structure or process which, when considered as a whole, is performing a function which the patent laws were designed to protect." *Diehr*, 450 U.S. at 191. Thus,

where the claim "wholly pre-empts" all uses of the natural phenomenon or abstract idea such that the "practical effect is a patent on the [phenomenon] itself' the claim is invalid under section 101. *Benson*, 409 U.S. at 71-72; *see also Diehr*, 450 U.S. at 187.

It is also important to note that "[p]atentability does not depend on which form the claim takes." *Nuijten*, 500 F.3d at 1362. As the Supreme Court has repeatedly explained, an "unpatentable principle" will not transform into a "patentable process" simply by adding conventional method steps. *Flook*, 437 U.S. at 588-90; *see also Diehr*, 450 U.S. at 191-92. If such were the case, "the determination of patentable subject matter [would] depend simply on the draftman's art." *Id.* at 593.

Whether a patent claim is invalid for failure to comply with section 101 is a question of law appropriate for summary judgment. *AT&T Corp. v. Excel Comm. Inc.*, 172 F.3d 1352, 1355 (Fed. Cir. 1999). When conducting the section 101 analysis, the claims must be examined "as a whole." *Diehr*, 450 U.S. at 188. The Supreme Court has specifically cautioned that it is "inappropriate to dissect the claims into old and new elements and then to ignore the presence of the old elements in the analysis." *Id.* at 188. Moreover, it is improper to consider the "novelty" of an element or step in a process claim. *Id.* at 188-89. Instead, novelty is a separate requirement set forth in 35 U.S.C. § 102.

Finally, Defendants who are challenging the validity of the claims of the patents-in-suit must show that the claims at issue are invalid by clear and convincing evidence. *Minnesota Mining and Mfg. Co. v. Chemque Inc.*, 303 F.3d 1294, 1301 (Fed. Cir.

2002). Thus, Defendants must show by clear and convincing evidence that the claims at issue (1) recite a "natural phenomenon," and (2) "wholly pre-empt" use of said phenomenon.

B. Analysis

Defendants contend that (1) the patents-in-suit claim the "correlation between the recited metabolite levels and therapeutic efficacy and/or toxicity" which is an unpatentable "natural, observable phenomenon"; and (2) the patents impermissibly preempt use of the correlation. Doc. No. 502 at 11, 13.

1. Recitation of Unpatentable Natural Phenomena

The first step in determining patentability under section 101 is to determine whether the claims "recite" a "natural phenomenon." *See Diehr*, 450 U.S. at 187; *see also In re Meyer*, 688 F.2d 789, 795 (C.C.P.A. 1982). For the reasons set forth below, this Court finds the patents-in-suit claim the correlations between certain thiopurine drug metabolite levels and therapeutic efficacy and toxicity, and said correlations are natural phenomena.

a. The Patents-in-Suit Recite the Correlations

Defendants assert that the patents-in-suit recite the correlation between thiopurine drug metabolite levels on the one hand and therapeutic efficacy and toxicity on the other. *See* Doc. No. 502 at 11-12. According to Defendants, the patents contain these correlations in the "wherein" clauses at the end of each claim. Though the "wherein" clauses are pre-

ceded by two steps – (1) "administering" a drug and (2) "determining" metabolite levels – Defendants argue that because both these steps have been performed in the prior art for decades, and each is a necessary step to making any use of metabolite levels, the claims cover the correlations themselves. Plaintiff counters that the claims at issue do not "recite" the correlations, rather the claims recite treatment methods which do not run afoul of section 101. *See* Doc. No. 528 at 1 n.1, 13.

Plaintiff has framed the patents-in-suit as treatment methods in that the claims purport to cover a "method for optimizing therapeutic efficacy" and/or "reducing toxicity" in patients taking AZA drugs for treatment of either gastrointestinal autoimmune diseases or nongastrointestinal autoimmune diseases. For example, Claim 1 of the '302 patent states:

1. A method of optimizing therapeutic efficacy for treatment of an immune mediated gastrointestinal disorder, comprising:

(a) administering a drug providing 6-thioguanine to a subject having said immune-mediated gastrointestinal disorder; and

(b) determining the level of 6-thioguanine in said subject having said immune-mediated gastrointestinal disorder wherein the levels of 6-thioguanine less than about 230 pmol per 8x108 red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject and wherein the levels of 6-thioguanine greater than about 400 pmol per 8x108 red blood

cells indicates a need to decrease the amount of said drug subsequently administered to said subject.

In the summary judgment order filed November 22, 2005, this Court construed the "indicates a need" language found in the "wherein" clause to mean "when the identified metabolites reach the specified level, the doctor is warned or notified that a dosage adjustment may be required." Doc. No. 227 at 17. As construed, the claims have three steps: (1) administer the drug to a subject; (2) determine metabolite levels; and (3) be warned that an adjustment in dosage may be required.

However, the fact that the inventors have framed the claims as "treatment methods" does not make the claims patentable. Indeed, "one can reduce any process to a series of steps. The question is what those steps embody." *Lab. Corp. of Am. Holdings v. Metabolite, Inc.*, 126 S.Ct. 2921 (2006) (Breyer, J., dissenting from dismissal of certiorari) (emphasis in original); *see also In re Grams*, 888 F.2d 835, 839 (Fed. Cir. 1989) (explaining that the critical question is: "What did applicants invent?") (quoting *In re Abele*, 684 F.2d 902, 907 (C.C.P.A. 1982)).

Here, a careful review of the claims of the patents-in-suit reveals that the steps embody only the correlations themselves. First, the "administering" and "determining" steps are merely necessary data-gathering steps for any use of the correlations. However, an "unpatentable principle" will not transform into a "patentable process" simply by adding conventional method steps. *Flook*, 437 U.S. at 588-90; *accord Meyer*, 688 F.2d at 794 ("[data-gathering] step[s] cannot make an otherwise nonstatutory claim statutory"). Thus, the Court must look to the third step to

determine what the applicants claim to have invented. However, as construed, the final step – the "warning" step (i.e. the "wherein" clause) – is only a mental step. That is, the "warning" step does not require that dosage be adjusted, or any other action. Indeed, contrary to Plaintiff's assertion, the "warning step" does not require that the doctor (or any person) "provide" a warning. *See* Doc. No. 528 at 14. Rather, it is the metabolite levels themselves that "warn" the doctor that an adjustment in dosage may be required.

Thus, the claims include only two active steps: "administering" the drug and "determining" metabolite levels, which are merely data-gathering steps; plus the additional mental step that the doctor be warned (by the metabolite levels) that an adjustment in dosage may be required. Therefore, the claims recite the correlations themselves. That is, what the inventors claim to have discovered is that particular concentrations of 6-TG and 6-MMP correlate with therapeutic efficacy and toxicity in patients taking AZA drugs.

b. The Correlations Are Natural Phenomena

Because the patents-in-suit claim the correlations, the Court must next determine whether the correlations are "natural phenomena." Defendants argue that the correlation between thiopurine drug metabolite levels and therapeutic efficacy and toxicity results from innate metabolic activity in the human body, and the correlations are therefore "natu-

ral phenomena." Doc. No. 542 at 5.[4] Plaintiff counters that the claimed correlations cannot be natural phenomena because the correlations would not have existed without the intervention of man-made drugs.[5] Doc. No. 528 at 8.

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[4] Doc. No. 542 is Defendants' reply in support of their motion for summary judgment of patent invalidity. Defendants submitted, in support of their reply brief, the declaration of Dr. Bruce Bostrom, which declaration Plaintiff separately moves to strike. *See* Doc. No. 549. Specifically, Plaintiff contends (1) Dr. Bostrom presents purely expert opinion but was not disclosed as an expert witness during discovery; (2) to the extent Dr. Bostrom's declaration is factual, Defendants also never disclosed him as a fact witness during discovery; and (3) Defendants should have presented the declaration with their moving papers and the late presentation is prejudicial to Plaintiff. Plaintiff argues that the declaration should be stricken for any of these reasons. *See id.* In the alternative, if the Court does not strike the declaration, Plaintiff requests it be permitted to file a sur-reply and attaches a proposed sur-reply to the motion as an exhibit. *See id.*, Exh. A. Defendants filed an opposition to Plaintiff's motion to strike and Plaintiff filed a reply to Defendants' opposition. However, this Court has not considered Dr. Bostrom's declaration in deciding the instant motion and, therefore, Plaintiff's motion to strike is DENIED as moot.

[5] Plaintiff contends "Congress has not excluded treatment methods or discovered correlations occurring from a man-made drug from patent protection and, in fact, has rejected proposed legislation to make treatment methods unpatentable. *Id.* (citing Morgan Decl., Exh. 11 (1995 Cong. U.S. HR 1127 (104th Congr., 1st Sess.)). The bill proposed that "a patent may not be issued for any invention or discovery of a technique, method, or process for performing a surgical or medical procedure, administering a surgical or medical therapy, or making a medical diagnosis, except that if the technique, method, or process is performed by or as a necessary component of a machine, manufacture, or composition of matter or improvement thereof which is itself patentable subject matter, the patent on such machine,

This Court finds that there can be little doubt that the claimed correlations are "natural phenomena." According to Plaintiff's own expert, Dr. Bloomfield, "the key therapeutic aspect of such thiopurine drugs is that they are converted ***naturally*** by enzymes within the patient's body to form an agent that is therapeutically active." Doc. No. 542, Exh. R ¶ 15 (emphasis added). Moreover, Dr. Seidman, one of the patents' inventors, concedes that the inventors merely observed these natural correlations by studying a "database of patient's information" which included patients taking 6-MP drugs. *See* Doc. No. 502, McClenahan Decl., Exh. K at 103-105. Dr. Seidman further testified that he believes the correlation still exists in the current patient population. Thus, the inventors of the patents-in-suit did not "invent" the claimed correlation. Rather, 6-TG and 6-MMP are products of the natural metabolizing of thiopurine drugs, and the inventors merely observed the relation ship between these naturally produced metabolites and therapeutic efficacy and toxicity.

The case law supports this conclusion. In *Funk Bros.*, for example, an inventor discovered a previously unknown feature of certain types of bacteria – that they could, "by certain methods of selection

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manufacture, or composition of matter may claim such technique, method, or process." 1995 Cong. HR 1127 (104th Congr., 1st Sess.). However, Defendants, in reply, urge the Court to ignore this irrelevant point because the failure to enact this legislation provides no support for the validity of the claims at bar. Doc. No. 542 at 14. This Court agrees with Defendants. The fact that Congress rejected legislation making treatment methods unpatentable is irrelevant, and not an appropriate basis for a determination of Congressional intent.

and testing, be isolated and used in mixed cultures" without inhibiting the properties of one another. 333 U.S. at 130. The patents at issue in that case claimed an inoculant for crops comprising a combination of these bacteria. *Id.* at 128, n.1. The Supreme Court held the claims invalid. The Court explained that the inventor did not "create" the "state of inhibition or non-inhibition in bacteria." *Id.* at 130. Rather, "[t]heir qualities are the work of nature." *Id.*

The same is true in the present case. The inventors here did not "create" the correlation between thiopurine drug metabolite levels and therapeutic efficacy and toxicity. Instead, the correlation results from a natural body process, which as the inventors concede, was pre-existing in the patient population, and it exists in the patient population today. Thus, just as in *Funk Bros.*, the claimed correlations are "the work of nature."

The facts of the present case are also similar to those of *Lab. Corp.*[6] The patent in *Lab. Corp.* claimed a method of measuring the level of an amino acid, called homocysteine, in the blood, which correlated with a deficiency in two vitamins: cobalamin

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[6] The Court takes note of Plaintiff's objections to the *Lab Corp.* opinion, namely that the opinion is not binding precedent and the dissent was issued on an incomplete record. And although at the time of the hearing on Defendants' motion this Court was not of the opinion that *Lab. Corp.* is directly relevant, after further review, this Court now finds that while *Lab. Corp.* does not hold precedential value, its reasoning is persuasive and relevant. A review of the case law in this area reveals that *Lab Corp.* is the case that is most factually similar to the present case. Thus, the Court would be remiss to ignore the case entirely.

and folate. *Lab. Corp.*, 126 S.Ct. at 2923-24. At the trial level, Lab. Corp. (the alleged infringers) did not argue invalidity under section 101, and instead based their invalidity arguments on other grounds. *See Metabolite Labs., Inc. v. Lab. Corp. of Am. Holdings*, 370 F.3d 1354 (Fed. Cir. 2004). The Federal Circuit, on appeal, rejected the invalidity arguments without addressing section 101. *Id.* The Supreme Court granted certiorari in order to determine whether the claim was invalid on the grounds that it improperly seeks to "claim a monopoly over a basic scientific relationship," Pet. for Cert. i, namely, the relationship between homocysteine and vitamin deficiency. *Lab. Corp.*, 126 S.Ct. at 2922. However, the Court never reached the issue because the writ was subsequently dismissed as improvidently granted apparently because the issue was not raised below. *Id.*

Nonetheless, Justice Breyer (joined by Justices Stevens and Souter), dissented from the dismissal of certiorari, and presented a lengthy dissenting opinion explaining why the patent should be found invalid under section 101. *See id.* at 2922-29. Justice Breyer, after reviewing the relevant cases in the subject area, stated:

> Even were I to assume (purely for argument's sake) that [the claim] meets certain general definitions of process patentability, however, it still fails the one at issue here: the requirement that it not amount to a simple natural correlation, *i.e.*, a 'natural phenomenon' . . .
>
> At most, respondents have simply described the natural law at issue in the abstract patent language of a 'process.' But they cannot avoid

> the fact that the process is no more than an instruction to read some numbers in light of medical knowledge. One might, of course, reduce the 'process' to a series of steps, *e.g.*, Step 1: gather data; Step 2: read a number; Step 3: compare the number with the norm; Step 4: act accordingly. But one can reduce *any* process to a series of steps. The question is what those steps embody. And here, aside from the unpatented test, they embody only the correlation between homocysteine and vitamin deficiency that the researchers uncovered. In my view, that correlation is an unpatentable 'natural phenomenon' and I can find nothing in [the claim] that adds anything more of significance.

Id. at 2928 (Breyer, J., dissenting from dismissal of certiorari) (internal citations omitted) (emphasis in original).

Although this Court notes that the dissent in *Lab. Corp.* does not have precedential value, the Court finds Justice Breyer's reasoning persuasive. Indeed, the claims in the patents-in-suit are clearly analogous to the claim in *Lab. Corp.* The claim at issue in *Lab Corp.* comprised two steps: "[(1)] assaying a body fluid for an elevated level of total homocysteine; and [(2)] correlating an elevated level of total homocysteine in said body fluid with deficiency of cobalamin or folate." *Id.* at 2924. The "assaying" step in *Lab Corp.* is akin to the "administering" and "determining" steps in the claims of the patents-in-suit as both are necessary steps for any use of the correlations. Similarly, *Lab Corp.'s* "correlating" step is akin to the "wherein" clause in the present case as both

recite the claimed correlation. Thus, the same reasoning that led Justice Breyer to conclude that the correlation between elevated homocysteine levels and deficiency of cobalamin or folate is a natural phenomenon supports the finding that the correlation between thiopurine drug metabolite levels and therapeutic efficacy and toxicity is a natural phenomenon.

Plaintiff argues, however, that the claimed correlations cannot be found to be natural phenomena because the correlations would not have existed without the intervention of man-made drugs. Plaintiff points out that thiopurine drugs are man-made drugs. Doc. No. 528 at 10. When these drugs are introduced into the body, they metabolize "to form an 'active metabolite' which then treats the patient's disease." *Id.* at 10-11. Thus, according to Plaintiff, because "the 6-TG and 6-MMP metabolites do not naturally exist in the body . . . [and would not exist] but for the administration of a man-made drug" the claimed correlations cannot be deemed "natural phenomena." *Id.* at 11. In support of this argument, Plaintiff cites to cases where courts have upheld as patentable claims involving the efficacy of man-made compositions, *see e.g.*, *Merck & Co. v. Teva Pharm., Inc.*, 347 F.3d 1367, 1369, 1372 (Fed. Cir. 2003), as well as claims involving portions of genes and proteins (which do not exist in nature). *See e.g.*, *Fiers v. Revel*, 984 F.2d 1164, 1166, 1172 (Fed. Cir. 1993).

However, in the Court's view, the cases Plaintiff cites do not support the patentability of the claims because the claims in the present case, unlike the claims in the cases cited by Plaintiff, do not cover the man-made compositions themselves or use of

man-made compositions to treat inflammatory bowel disease or autoimmune diseases. In *Merck*, for example, the claims covered a method for treating osteoporosis through the administration of a bisphosphonic acid, a man-made composition. 347 F.3d at 1369. The claims at issue in that case specifically covered use of the acid in the treatment method. *Id.* at 1369. This contrasts with the present case where the claims cover the correlations themselves, rather than use of the man-made composition to treat the targeted disease, as this Court has already found. Because the patents-in-suit claim the correlations, the relevant inquiry is whether the correlations are "man-made," not whether a man-made drug was used to produce the correlation.[7]

Again, the present case is most similar to *Funk Bros.* In that case, the claimed combination of bacteria was "man-made." That is, the claimed strains of bacteria had to be manually isolated and mixed, and therefore would not exist in nature without human intervention. 333 U.S. at 130. Despite this human intervention, the claim was nonetheless unpatentable under section 101. *Id.* at 132. As such, per *Funk Bros.*, claims do not gain patentability simply by including man-made compositions. Thus, the patents-in-suit do not gain patentability solely by virtue of the fact that man-made drugs are used in connection with the claimed correlation.

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[7] This same reasoning makes *Fiers* inapposite as well. Plaintiff cites to *Fiers* merely because it involved man-made compositions – purified DNA. Plaintiff argues that if claims to portions of genes and proteins (which do not exist in nature) are not "natural phenomenon" then the correlations cannot be "natural phenomenon" either. Doc. No. 528 at 11.

The recent Federal Circuit case, *Nuijten*, further supports this finding. *Nuijten* concerned a patent application which disclosed "a technique for reducing distortion induced by the introduction of 'watermarks' into signals." 500 F.3d at 1348. The court analyzed whether *Nuijten's* "signal claim" fell within any of the four statutory classes of patentable subject matter: process, machine, manufacture, or composition of matter. *Id.* at 1353. Ultimately, the court concluded that the claim was unpatentable because it did not fit within any of the statutory categories. *Id.* at 1357. In ruling that the claim was not a "manufacture" the court explained that the claimed signal was "man-made, in the sense of having been encoded, generated, and transmitted by artificial means," however "artificiality is insufficient by itself to render something a 'manufacture.'" *Id.* at 1356. Thus, the fact that the claimed signal was "man-made" did not automatically make the claim patentable. To the contrary, although the claimed signal was "man-made," it was still unpatentable.[8]

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[8] Plaintiff's argument that *Nuijten* is "irrelevant to the present case" is to no avail. Doc. No. 588 at 25. Plaintiff would have the Court believe that the *Nuijten* holding "had nothing to do with whether or not the claimed subject matter was 'man-made.'" *Id.* This is incorrect. The Federal Circuit's finding that the claimed signal was "man-made" and yet not a "manufacture," was one of several reasons why the court ultimately determined that the claim was unpatentable. Thus, *Nuijten* confirms that claims do not gain patentability simply because they incorporate something that is "man-made." Finally, Plaintiff's argument that *Nuijten* is irrelevant because the present case recites "a process" is similarly unpersuasive. As the Court already found, although the patents-in-suit are framed as "method claims," they claim the correlations themselves.

In short, the correlation between particular 6-TG and 6-MMP metabolite levels and therapeutic efficacy and toxicity is not an "invention." Rather, 6-TG and 6-MMP are products of the natural metabolizing of thiopurine drugs, and the inventors merely discovered the relationship between these naturally produced metabolites and therapeutic efficacy and toxicity.

2. Preemption

Because the Court has determined that the claims of the patents-in-suit recite a natural phenomenon, the Court must next determine whether the claims "wholly pre-empt" use of the natural phenomenon such that the "practical effect is a patent on the [phenomenon] itself." *Benson*, 409 U.S. at 71-72; *see also Diehr*, 450 U.S. at 187. Defendants argue that because the "administering" and "determining" steps are necessary to using the correlations, Plaintiff's claims "wholly pre-empt" use of the correlations in violation of Supreme Court precedent, and are thus invalid under section 101. Doc. No. 502 at 13-14. In opposition, Plaintiff argues first, that the relevant tests is the alternative "transformation/results" test not the preemption test. *See* Doc. No. 528 at 7-8. Second, even if the Court applies the preemption test, the claims do not "wholly pre-empt" all uses of the correlations. This Court finds that (a) the preemption test is the relevant test and (b) Plaintiff's claims "wholly pre-empt" use of the correlations.

a. The Preemption Test

The case law is clear, if a claim that recites unpatentable subject mater "wholly pre-empts" all practical use of the unpatentable subject matter, the

claim is invalid under section 101. *Benson*, 409 U.S. at 71-72; *see also Diehr*, 450 U.S. at 187. *Benson* involved an attempt to patent "a method of programming a general-purpose digital computer to convert signals from binary-coded decimal form into pure binary form." *Id.* at 65. The conversion was achieved through use of an algorithm, defined as "[a] procedure for solving a given type of mathematical problem." *Id.* at 67. The claims "were not limited to any particular art or technology, to any particular apparatus or machinery, or to any particular end use." *Id.* at 64. The Supreme Court concluded that because the claimed process "has no substantial practical application except in connection with a digital computer" the patent "would wholly pre-empt the mathematical formula and in practical effect would be a patent on the algorithm itself." *Id.* at 71-72. For this reason, the Court held the patent invalid. *Benson* is binding Supreme Court precedent, and the preemption test articulated therein is clearly applicable to the present case.

Moreover, contrary to Plaintiff's contention, Defendants need not meet the additional burden of showing that the claims do not "transform" an article or physical object to a different state or thing and/or do not produce a "useful, concrete and tangible result." Doc. No. 528 at 7-8 (citing *AT&T*, 172 F.3d at 1357-58). The case law in this area reveals that the additional showing urged by Plaintiff is not required. In *Flook*, for example, the Supreme Court did not even mention the alternative transformation/result standard, and instead focused on whether the claims "wholly pre-empt" all uses of the natural phenome-

non. 437 U.S. at 589-90.[9] Also, although *Comiskey* mentions the "transformation" test, it does so in regards to process patents reciting algorithms or abstract concepts in claims directed to industrial processes. Such claims clearly differ from those in the present case. The *Comiskey* court specifically noted that "process claims not limited to claiming an abstract concept or algorithm (i.e., a mental process) **may not be subject to the same requirements.**" 499 F.3d at 1377 n.12 (emphasis added).

As for the "useful, concrete and tangible result" standard, the Supreme Court has never applied that standard. *See Lab. Corp.*, 126 S. Ct. at 2928 (pointing out that the Supreme Court has never held "that a process is patentable if it produces a 'useful, concrete, and tangible result' . . . and if taken literately, the statement would cover instances where this Court has held the contrary") (Breyer, J., dissenting). Furthermore, while the Federal Circuit has applied the standard, it has always done so in the context of computer-related inventions involving algorithms for data manipulation. *See e.g.*, *State Street Bank and Trust Co. v. Signature Fin. Group, Inc.*, 149 F.3d 1368 (Fed. Cir. 1998).

Thus, this Court finds that the claims at issue are not subject to either the transformation test or the "useful, concrete and tangible" result test.

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[9] During oral argument, Plaintiff argued that *Flook* was "overruled" by the Supreme Court in *Diehr*. *See* May 10, 2007 Hearing Transcript at 38:14-24. However, in *Comiskey*, the Federal Circuit repeatedly cited *Flook* and also explained the case. 499 F.3d at 1371, 1375, 1376, 1377-78. This confirms that *Flook* remains good law.

b. The Claims "Wholly Pre-empt" the Use of the Correlation

Defendants argue that the claims "wholly pre-empt" use of the correlation because the only practical use of the correlation is in drug treatment for gastrointestinal autoimmune diseases and non-gastrointestinal autoimmune diseases, and anyone seeking to employ the correlation must conduct the only active steps recited in the claims – administer the drug and determine metabolite levels. Doc. No. 502 at 13-15. This Court agrees.

This Court has already found that the claims recite the correlations. Specifically, the Court has found that the "administering" and "determining" steps are merely necessary data gathering steps for any use of the correlations, and the "warning" step is only a mental step whereby the metabolite levels warn the doctor that an adjustment in dosage may be required. Thus, the claims cover the correlations themselves. That is, what the inventors claim to have discovered is that particular concentrations of 6-TG and 6-MMP correlate with therapeutic efficacy and/or toxicity in patents taking AZA drugs. Because the claims cover the correlations themselves, it follows that the claims "wholly pre-empt" the correlations.

For the same reason, the Court rejects Plaintiff's argument that it may preclude others from using the correlations "in conjunction with all the other steps in their claimed process." Doc. No. 528 at 19 (citing *Diehr*, 450 U.S. at 187; *Arrhythmia Research Tech., Inc. v. Corazoniz Corp.*, 958 F.2d 1053, 1059 (Fed. Cir. 1992)). Again, the only "other steps" re-

cited in the claims are the "administering" and "determining" steps, which are necessary data-gathering steps. And, the inclusion of such steps cannot "transform an unpatentable principle into a patentable process." *Diehr*, 450 U.S. at 191-192.

The Court also finds Plaintiff's supposed examples of other permissible uses of the correlations unavailing. Doc. No. 528 at 19-20. First, the law does not require that every conceivable use be preempted to invalidate the claim. Rather, it is enough that the unpatentable subject matter recited in the claims has "no substantial practical application" outside the context of the claims. *Benson*, 409 U.S. at 71-72. In *Benson*, the Court found that the mathematical formula involved in that case had "no substantial practical application except in connection with a digital computer." *Id.* Thus, a patent which claimed "a method of programming a general-purpose digital computer to convert signals from binary-coded decimal form into pure binary form" through the use of a mathematical formula would "wholly pre-empt the mathematical formula and in practical effect would be a patent on the algorithm itself." *Id.* at 65, 71-72. The same is true in the present case. Because the correlations have "no substantial practical application" outside of the treatment for immune mediated gastrointestinal disorders and autoimmune diseases, it does not matter that uses outside of this context are not foreclosed.

Second, the alternate uses cited by Plaintiff as not being preempted do not change the fact that the "practical effect" of the patent would be a "patent on the [phenomenon] itself." *Id.* at 72. Plaintiff outlines six possible uses not foreclosed by the claimed me-

thods: (1) use in research; (2) for diseases other than autoimmune or gastrointestinal diseases;[10] (3) use when results are given in units other than red blood cells; (4) building upon the correlations; (5) publishing articles in scientific journals concerning the correlations; and (6) testing and determining metabolite levels so long as no warning is given. Doc. No. 528 at 20. None of these uses, however, make the subject claims patentable. In *Benson*, the claimed algorithm could have been used in research and scientific journals could have published articles about it, however, the claim was still invalid. Also, as discussed above, there are no known practical uses other than treatment for autoimmune or gastrointestinal diseases. Thus, the fact that uses for other diseases are not foreclosed, if true, is of no consequence. Finally, that testing and determining metabolite levels is not preempted "so long as the doctors are not warned that doses may need to be adjusted" does not aid Plaintiff's argument because under this scenario the correlations would not be used at all. Thus, despite these supposed alternate uses, the claims "wholly pre-empt" use of the correlation such that the "prac-

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[10] The Court notes that Plaintiff's position taken here is inconsistent with the record in this case. Plaintiff has accused Defendants' researcher, Dr. Rokea el-Azhary, of infringement for conducting a study to determine whether there were different correlations for dermatologic diseases than for gastrointestinal diseases. Plaintiff's expert opined that this research amounted to infringement, and at oral argument, Plaintiff argued that its claims covered dermatologic diseases. *See* May 10, 2007 Hearing Transcript at 21:10-13.

tical effect is a patent on the [correlation] itself." *Benson*, 409 U.S. at 71-72.[11]

3. *In re Comiskey* Cannot Save Plaintiff's Claims

The recent Federal Circuit case *In re Comiskey* does not change the result. Plaintiff argues that even if the Court determines that the correlations are natural phenomena, *Comiskey* demonstrates that the inclusion of patentable subject matter (i.e. machines) in the claim makes the claims patentable under section 101. Doc. No. 593 at 1. The Court disagrees. First, this Court notes that *Comiskey* is not directly on point because the facts of that case are wholly dissimilar from the facts of the present case. Second, contrary to Plaintiff's argument, *Comiskey* does not hold that the inclusion of a machine in the claim au-

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[11] Plaintiff seeks to bolster its claims by distinguishing *Benson* and instead relying on *Chakrabarty* and *Arrhythmia*. *See* Doc. No. 528 at 21. Plaintiff argues that *Benson* is inapplicable because the claim in that case was only to the mathematical algorithm and included no limitation to any art, technology, or use. *Id.* Instead, Plaintiff points to *Chakrabarty* and *Arrhythmia* as support for its argument that the claims do not wholly preempt use of the correlations. However, this Court has already held that the claims in this case, similar to the claims in *Benson*, are only to the correlations themselves. Moreover, *Chakrabarty* is distinguishable on its facts. The claims in that case were to a new, non-naturally occurring bacterium. Conversely, in the present case the inventors did not invent a new organism, rather, they merely discovered an unpatentable natural correlation. *Arrhythmia* is also inapposite. In that case the court applied the so-called *Freeman-Walter-Abele* test, which the Federal Circuit has since held "has little, if any, applicably to determining the presence of statutory subject matter." *See Arrhythmia*, 958 F.2d at 1059-60; *State Street*, 149 F.3d at 1374.

tomatically makes the claims patentable. Third, if the Court were to apply the *Comiskey* analysis to the present case, the claims of the patents-in-suit are still unpatentable under section 101.

Comiskey involved an application for a business method patent on a system of mandatory arbitration of disputes involving legal documents such as wills and contracts. 499 F.3d at 1368. Some of the claims contained multiple mental steps, but did not require the use of any technology, while other claims required the use of a computer or other device to perform the steps of the method. *Id.* at 1369, 1379. Indeed, the later claims recited the use of technology in the claims themselves: "wherein access to the mandatory arbitration is established through the Internet, intranet, World Wide Web, software applications, telephone, television, cable, video [or radio], magnetic, electronic communication, or other communication means." *Id.* at 1379. The Federal Circuit reviewed the claims for compliance with section 101, and held that the claims which did not require the use of a computer amounted to abstract mental processes that could not be patented under section 101. *Id.* at 1381. At the same time, however, the court held that the claims which required the use of a computer or other device claimed patentable subject matter under section 101 (though the claims were remanded so the Patent Office could determine whether the use of the technology would have been non-obvious under 35 U.S.C. § 103). *Id.* In reaching this decision, the court explained that "while the mere use of the machine to collect data necessary for application of the mental process may not make the claim patentable subject matter, these claims in combining the use of machines with a mental

process, claim patentable subject matter." *Id.* at 1380 (citations omitted). Thus, the distinction between the patentable claims and the unpatentable claims was whether the claims were "tied to a particular apparatus." *Id.* at 1379.

Relying on *Comiskey*, Plaintiff argues that the patents-in-suit meet the requirements of section 101 because the claims "involve specific machines." Doc. No. 593 at 2. According to Plaintiff, the asserted claims of the patents-in-suit "inherently require" the use of "specific machines" to detect the levels of metabolites. Doc. No. 588 at 14. "These machines include a detector, a pump and an injector." *Id.* Moreover, Plaintiff asserts, "dependent claims 6, 14, 24, 30 and 53 of the '623 Patent expressly require the use of a machine capable of performing high pressure liquid chromatography (HPLC)." *Id.* Thus, according to Plaintiff, the claims are patentable.

However, even assuming *arguendo* that *Comiskey* is applicable, Plaintiff's reading of the case is too broad. Plaintiff would have the Court find that under *Comiskey*, any "involvement" of a machine or composition of matter in a method claim is enough to render the claims patentable under section 101. *See id.* at 1. However, prior case law suggests that this is not the rule. Instead, the Supreme Court has previously held claims unpatentable under section 101 even though they "involve" a machine or composition of matter. In *Flook* the Supreme Court held claims invalid under section 101 even though they involved the catalytic chemical conversion of hydrocarbons, which are compositions of matter. 437 U.S. at 596. Similarly, in *Benson* the patentees sought to claim "a method of programming a general-purpose digital

computer to convert signals from binary-coded decimal form into pure binary form," and despite the clear involvement of a computer, the Court held the claims unpatentable under section 101. 409 U.S. at 65. The Federal Circuit has done the same. In *Grams* the court held claims unpatentable under section 101 even though one step of the claim required the use of a machine. 888 F.2d at 836. In that case the claims covered a "method of diagnosing an abnormal condition in an individual." *Id.* The first, and only physical, step in the claim was "performing clinical tests on individuals to obtain data." *Id.* at 840. The clinical tests were "produced by a standard chemical analyzer that measures the levels of the chemical biological components," i.e. a machine. Nonetheless, the Federal Circuit held the claims unpatentable under section 101. The difference between those cases and *Comiskey* is that in *Flook*, *Benson* and *Gram* the use of the machine or composition of matter was merely incidental, while in *Comiskey* the machine was "tied to" the operation of the claim and in fact recited in the claim. Thus, the better reading of *Comiskey* is that claims which are "tied to a particular apparatus" may be invalid, while claims that involve machines in a merely incidental fashion are not foreclosed.

Applying *Comiskey* to the present case, the patents-in-suit would be invalid if the claims were "tied to a particular apparatus." However, this is not the case. Rather, the machines identified by Plaintiff are merely incidental to the claims just as in *Flook*, *Benson* and *Grams*. The present case is most similar to *Grams* as the "determining" step in the present case is analogous to the "performing" step in *Grams*. In both instances, the mere involvement of a machine in a data-gathering step cannot render the claim statu-

tory. *See Grams*, 888 F.2d at 840. Moreover, the patents-in-suit are easily distinguishable from the claims at issue in *Comiskey*. In *Comiskey*, the use of technology was explicitly recited in the claims. *See id.* at 1379. However, the patents-in-suit do not even mention any machines, thus it would be disproportionate to conclude that the claims are "tied to a particular apparatus." It follows that even applying *Comiskey*, the claims of the patents-in-suit are invalid under section 101.

4. There Are No Genuine Issues of Material Fact Precluding Summary Judgment

In its final effort, Plaintiff argues that there are four underlying factual issues precluding summary judgment in Defendants' favor: (1) whether the claims at issue claim a "natural phenomenon"; (2) whether the claims at issue transform an article into a different state or thing; (3) whether the claims at issue produce a useful, concrete, and tangible result; and (4) whether the claims at issue "wholly preempt" all uses of the inventors' correlation. Doc. No. 528 at 27. However, these issues do not represent factual disputes, and instead concern interpretation of the claims and the proper application of section 101 to the facts of this case. These are clearly questions of law, and are thus appropriate for summary judgment. *See AT&T Corp.*, 172 F.3d at 1355 (explaining that whether a patent claim is invalid under section 101 is a question of law appropriate for summary judgment).

5. *Conclusion*

Based on the foregoing, this Court finds that there is no genuine issue of material fact to be resolved as to whether the patents-in-suit are directed to statutory subject matter in compliance with 35 U.S.C. § 101. This Court finds by clear and convincing evidence that the patents-in-suit recite a natural phenomenon – the correlations between thiopurine drug metabolite levels and therapeutic efficacy and/or toxicity – and the claims "wholly pre-empt" use of said correlations. Therefore, the claims are invalid under section 101.

CONCLUSION AND ORDER

Accordingly, IT IS HEREBY ORDERED that Defendants' motion for summary judgment on patent invalidity pursuant to 35 U.S.C. § 101 is **GRANTED**.

IT IS FURTHER ORDERED that:

1. Plaintiff's motion for summary judgment of no patent exhaustion is **DENIED as moot.**
2. Plaintiff's motion for summary judgment for declaratory infringement of patent nos. 6,355,623 and 6,680,302 is **DENIED as moot.**
3. Plaintiff's motion to strike the declaration of Dr. Bruce Bostrom is **DENIED as moot.**

DATED: March 28, 2008

/s/
JOHN A. HOUSTON
United States District Judge

APPENDIX C

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF CALIFORNIA

Civil No. 04cv1200 JAH (RBB)

PROMETHEUS LABORATORIES, INC.,
Plaintiff,

v.

MAYO COLLABORATIVE SERVICES dba MAYO MEDICAL LABORATORIES AND MAYO CLINIC ROCHESTER,
Defendants

AND RELATED COUNTERCLAIM.

ORDER DENYING DEFENDANT'S MOTION FOR SUMMARY JUDGMENT [DOC #14] AND GRANTING PLAINTIFF'S CROSS-MOTION FOR SUMMARY JUDGMENT [DOC #135]

INTRODUCTION

This matter is now before the Court on the parties' cross-motions for summary judgment. The parties' motions have been fully briefed and oral argument was entertained. After a careful consideration of the pleadings and relevant exhibits submitted by the parties, the oral argument presented at the hearing, and for the reasons set forth below, this Court DENIES defendant's motion for summary judgment and GRANTS plaintiff's cross-motion.

BACKGROUND

1. Factual Background

Plaintiff is the exclusive licensee of two patents: U.S. Patent Nos. 6,355,623 ("the '623 patent") and 6,680,302 ("the '302 patent"). The patents-in-suit involve technology used in blood tests for the treatment of patients with various inflammatory bowel diseases and other autoimmune diseases. The patented technology provides the means for measuring the level of certain metabolites[1] in the blood in patients that were treated with thiopurine drugs, including the anti-Crohn's disease drug, azathioprine ("AZA"). The test using the patented technology ("the patented test") measures the level of two metabolites: 6-thioguanine ("6-TGN") and 6-methylmercaptopurine ("6-MMP"). The patented test for these metabolites measure patients' 6-TGN and 6-MMP, indicating that drug usage should be reduced at levels "greater than about 400" and "greater than about 7000," respectively, in order to avoid toxic side effects.

Defendant Mayo Collaborative Services dba Mayo Medical Laboratories ("defendant") developed a test ("the accused test") to measure the same metabolites but using different levels, 450 6-TGN and 5700 6-MMP. In June 2004, defendant announced it will begin to use its accused test, offering it for sale

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[1] Metabolites are compounds formed when the body breaks down a drug.

to potential purchasers.[2] The instant lawsuit followed.

2. Procedural History

Plaintiff filed its patent infringement complaint on June 15, 2004. Defendant filed an answer to the complaint, along with a counterclaim, on October 6, 2004. Plaintiff filed an answer to the counterclaim on October 29, 2004.

Defendant filed its motion for summary judgment on January 27, 2005, with the hearing initially scheduled for March 27, 2005. Plaintiff, on February 17, 2005, filed an *ex parte* application seeking to continue the hearing date for defendant's summary judgment motion in order to allow for a *Markman* hearing to be conducted. Plaintiff's *ex parte* application was subsequently denied but the Court rescheduled the summary judgment motion hearing to April 7, 2005. The parties then stipulated to continue the hearing until April 21, 2005. Plaintiff filed its opposition to defendant's summary judgment motion on March 24, 2005, under seal. Defendant's reply brief was filed on March 24, 2005.

On April 12, 2005, plaintiff filed objections to defendant's facts and evidence submitted in support of its motion for summary judgment. On April 21, 2005, defendant, in response, filed a motion to strike plaintiff's objections as untimely filed.[3] On April 15,

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[2] Defendant explained, during oral argument, that it rescinded its announcement after the inception of this lawsuit and the accused test has not been implemented as of the date of the hearing.

[3] Plaintiff filed its objections to the facts and evidence presented by defendant in support of its motion for summary

2005, plaintiff submitted an *ex parte* application for leave to file a sur-reply in further opposition to defendant's motion for summary judgment. Defendant opposed the *ex parte* request and plaintiff filed a reply to defendant's opposition to the request. The Court subsequently, on its own motion, rescheduled the April 21, 2005 motion hearing to June 16, 2005. Then, on May 12, 2005, the Court, again on its own motion, rescheduled the hearing until August 4, 2005.

On June 30, 2005, Magistrate Judge Ruben B. Brooks conducted a case management conference, during which the following orders were entered, among others:[4]

1. The hearing date on defendant's motion for summary judgment was rescheduled to September 15, 2005.
2. Plaintiff's cross-motion was set for hearing the same date and directed to be filed by August 4, 2005.
3. Plaintiff's request to file a supplemental opposition defendant's motion was

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judgment well after the deadline set for filing its opposition, in which such objections should have been presented. *See* CivLR 7.1 (e.2). Plaintiff does not present any reason to excuse the untimely filing. Accordingly, defendant's motion to strike plaintiff's objections to defendant's facts and evidence [doc. #73] is GRANTED.

[4] Judge Brooks also vacated the hearing date set for defendant's motion for leave to file an amended answer and counterclaim, taking that motion, along with plaintiff's motion seeking leave to file an amended complaint adding Mayo Clinic Rochester as a defendant, under submission without oral argument. The motions are currently pending before this Court.

granted and directed to be filed by August 4, 2005.

4. Defendant was granted the opportunity to file a supplemental reply to plaintiff's supplemental opposition. Defendant's supplemental reply and opposition to plaintiff's summary judgment motion was due by August 15, 2005.

5. Plaintiff's reply in support of its cross-motion was due by August 25, 2005.

6. Plaintiff's *ex parte* application to file a sur-reply was denied as moot.

Plaintiff filed its cross-motion, under seal, on August 9, 2005. On August 11, 2005, the Court, on its own motion, rescheduled the motion hearing on the cross-motions for summary judgment to September 29, 2005. Defendant filed an opposition to plaintiff's motion and a supplemental reply brief in support of its motion on August 19, 2005. Plaintiff filed its reply brief on September 2, 2005.

This Court entertained oral argument by the parties on September 29, 2005. Prior to commencement of oral argument, the Court unsealed all documents sealed in conjunction with these motions. At the conclusion of the hearing the Court directed the parties to submit rebuttal and supplemental briefing. Defendant filed its rebuttal brief on October 3, 2005. Plaintiff's supplemental brief was filed on October 4, 2005 and its sur-rebuttal brief was filed on October 7, 2005. Defendant's response to plaintiff's supplemental brief was also filed on October 7, 2005. On October 14, 2005, defendant submitted an *ex parte* application seeking leave to file a supplemental re-

sponse to plaintiff's Rule 56(f) supplemental brief. Plaintiff, on October 27, 2005, filed a rebuttal brief to defendant's supplemental response.

DISCUSSION

Defendant moves for summary judgment, contending there is no genuine issue of material fact to be resolved in this case and seeking a declaration of non-infringement of the patents-in-suit. Defendant contends that, when the patents-in-suit are properly construed, the accused test does not infringe plaintiff's patents, either literally or through the doctrine of equivalents. Plaintiff cross-moves for summary judgment, seeking a judicial declaration that defendant's accused test literally infringes Claim 7 of the '623 patent.

1. Summary Judgment Legal Standard

A moving party who demonstrates that the "pleadings, depositions, answers to interrogatories, and admissions on file, together with the affidavits, if any, show that there is no genuine issue as to any material fact" may be entitled to summary judgment as a matter of law under Fed. R. Civ. P. 56(c). The nonmoving party can defeat summary judgment by demonstrating that a material issue of fact exists. *See Celotex Corp. v. Catrett*, 477 U.S. 317, 322 (1986). A fact is material when it is outcome determinative. *Anderson v. Liberty Lobby, Inc.*, 477 U.S. 242, 248 (1986).

When ruling on a summary judgment motion, the Court must examine all the evidence in the light most favorable to the non-moving party. *Morgan v. United States*, 709 F.2d 580, 584 (9th Cir. 1983). The Court cannot engage in credibility determinations,

weighing of evidence, or drawing of legitimate inferences from the facts; these functions are for the jury. *Anderson*, 477 U.S. at 255.

A material fact is one that is relevant to an element of a claim or defense and the existence of which might affect the outcome of the suit. The materiality of a fact is thus determined by the substantive law governing the claim or defense. Disputes over irrelevant or unnecessary facts will not preclude a grant of summary judgment. *T.W. Electrical Service, Inc. v. Pacific Electrical Contractors Ass'n*, 809 F.2d 626, 630 (9th Cir. 1987) (citing *Anderson*, 477 U.S. at 248).

Entry of summary judgment is appropriate "against a party who fails to make a showing sufficient to establish the existence of an element essential to that party's case, and on which that party will bear the burden of proof at trial." *Celotex*, 477 U.S. at 322. Without specific facts to support the conclusion, a bald assertion of the "ultimate fact" is insufficient. *See Schneider v. TRW, Inc.*, 938 F.2d 986, 990-91 (9th Cir. 1991).

Cross-motions for summary judgment do not necessarily permit the judge to render judgment in favor of one side or the other. *Starsky v. Williams*, 512 F.2d 109, 112 (9th Cir. 1975). The Court must consider each motion separately "on its own merits" to determine whether any genuine issue of material fact exists. *Fair Housing Council of Riverside County, Inc. v. Riverside Two*, 249 F.3d 1132, 1136 (9th Cir. 2001); *Starsky*, 512 F.2d at 112. When evaluating cross-motions for summary judgment, the Court must analyze whether the record demonstrates the existence of genuine issues of material fact, both in

cases where both parties assert that no material factual issues exist, as well as where the parties dispute the facts. *See Fair Housing Council of Riverside County*, 249 F.3d at 1136 (citing *Chevron USA, Inc. v. Cayetano*, 224 F.3d 1030, 1037 & n.5 (9th Cir. 2000)).

2. Analysis

The parties' cross-motions each seek construction of various claim terms contained in the patents-in-suit, which is required in order for the Court to properly determine the issue of infringement. *See Liquid Dynamics Corp. v. Vaughan Company*, 355 F.3d 1361, 1367 (Fed. Cir. 2004) (in patent infringement cases, the Court first determines the meaning of the asserted patent claims, and then compares the properly construed claims to the allegedly infringing device). Because a determination of infringement requires that claim terms be properly construed, claims construction will be addressed first.

A. Claims Construction

1. Legal Standard

In order to determine the meaning of the asserted patent claims, the court considers "the evidence necessary to resolve disputes about claim terms and to assign a fixed, unambiguous, legally operative meaning to the claim." *Liquid Dynamics*, 355 F.3d at 1367. The terms of a claim are given their ordinary and customary meaning, determined from the view of a person of ordinary skill in the relevant art. *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005). The *Phillips* court explained:

> In some cases, the ordinary meaning of claim language as understood by a person of skill in the art may be readily apparent even to lay judges, and claim construction in such cases involves little more than the application of the widely accepted meaning of commonly understood words. In such circumstances, general purpose dictionaries may be helpful. In many cases that give rise to litigation, however, determining the ordinary and customary meaning of the claim requires examination of terms that have a particular meaning in a field of art. Because the meaning of a claim term as understood by persons of skill in the art is often not immediately apparent, and because patentees frequently use terms idiosyncratically, the court looks to 'those sources available to the public that show what a person of skill in the art would have understood disputed claim language to mean.' Those sources include 'the words of the claims themselves, the remainder of the specification, the prosecution history, and extrinsic evidence concerning relevant scientific principles, the meaning of technical terms, and the state of the art.'

Id. at 1314 (internal citations omitted).

"The plain and ordinary meaning of the claim language controls, unless that meaning renders the claim unclear or is overcome by a special definition

that appears in the intrinsic record with reasonable clarity and precision." *N. Telecom Ltd. V. Samsung Electronics Co.*, 215 F.3d 1281, 1295 (Fed Cir. 2000). In some cases, prosecution history can be useful to interpret claim terms, but "it cannot be used to limit the scope of a claim unless the applicant took a position before the PTO that would lead a competitor to believe that the applicant had disavowed coverage of the relevant subject matter." *Schwing GmbH v. Putzmeister Aktiengesellschaft*, 305 F.3d 1318, 1324 (Fed. Cir. 2002). Absent amendments to the patent claims, an applicant "must clearly and unambiguously express any such surrender of subject matter during prosecution." *Invitrogen Corporation v. Biocrest Manufacturing*, 327 F.3d 1364, 1367 (Fed. Cir. 2003); *see York Products, Inc. v. Central Tractor Farm & Family Center*, 99 F.3d 1568, 1575 (Fed. Cir. 1996).

2. Analysis

At issue in these cross-motions are Claim 1 of the '302 patent and Claim 7 of the '623 patent. Claim 1 of the '302 patent states:

> 1. A method of optimizing therapeutic efficacy for treatment of an immune-mediated gastrointestinal disorder, comprising:
>
> (a) administering a drug providing 6-thioguanine to a subject having said immune-mediated gastrointestinal disorder; and
>
> (b) determining the level of 6-thioguanine in said subject having said immune-mediated gastrointestinal disorder, wherein the level of 6-

thioguanine less than about 230 pmol per $8x10^8$ red blood cells indicates a need to increase the amount of said drug subsequently administered to said subject and *wherein the level of 6-thioguanine greater than about 400 pmol per $8x10^8$ red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.*

Bush Decl., Exh. G at 87 (emphasis added).

Claim 7 of the '623 patent states:

7. A method of reducing toxicity associated with treatment of an immune-mediated gastrointestinal disorder;

(a) administering a drug providing 6-thioguanine to a subject having said immune-mediated gastrointestinal disorder;

(b) determining the level of 6-thioguanine in said subject having said immune-mediated gastrointestinal disorder; and

(c) determining the level of 6-methyl-mercaptopurine in said subject having said immune-mediated gastrointestinal disorder, *wherein the level of 6-thioguanine greater than about 400 pmol per $8x10^8$ red blood cells or the level of 6-methyl-mercaptopurine greater than about 7000 pmol per $8x10^8$ red blood cells indicates a need to decrease*

the amount of said drug subsequently administered to said subject.

Bush Decl., Exh. A at 21 (emphasis added). In order to properly rule upon the issues presented in both motions[5] construction of the phrase "greater than about 400" as used in both patent claims is required. Plaintiff's motion also requires a proper construction of the phrase "indicates a need" as used in the '623 patent.

a. "Greater Than About 400"

Defendant's briefs center on construction of the "about 400" term contained in the patents-in-suit, contending that a proper construction of "about 400" would require a finding of non-infringement. *See, e.g.*, Deft's Mot. at 15-19; Reply at 5-6. Plaintiff, throughout its pleadings, notes that defendant's focus on the "about 400" language improperly ignores[6] the "greater than" language that must be considered in construing the claims at bar. *See, e.g.*, Pltff's Opp. at 15; Pltff's Suppl. Opp. at 15. This Court, after a thorough review of the patents at issue, finds that construction of both the "greater than" and "about 400" language is clearly required in order to properly construe the claims.

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[5] The parties have submitted voluminous briefs containing numerous arguments and evidence in support of their respective motions. This Court has thoroughly reviewed all arguments and relevant exhibits submitted. For the sake of brevity, this Order addresses only those arguments and evidence the Court deems relevant in determining the issues presented.

[6] As discussed later, defendant did present arguments during the hearing in opposition to plaintiff's proposed construction of the "greater than" language.

1. "Greater Than"

Plaintiff contends that the "greater than" language "simply means any value larger than about 400 with the understanding that the risk of toxicity increases as the 6-TG[7] level increases." Pltff's Suppl. Opp. at 15. Although defendant fails to address the "greater than" language in any of its briefs, at oral argument, defendant contends that the "greater than" language cannot be construed as covering all levels higher than "about 400" because there is no upper limit on the level of metabolites and, thus, if the "greater than" language is construed to mean any number higher or more than "about 400," the patents would improperly cover an indefinite number.

Plaintiff explains that no upper limit was required to be disclosed because "[l]evels of 500, 600 or more are still potentially toxic ... [for example] 6-TGN levels of '490' in adults correlate with hematologic toxicity." Pltff's Suppl. Opp. at 14 (citing Bloomfeld Decl., Exh. 1 ('623 Patent) at 32 (Example II). Plaintiff further explains that there is no reason for an upper limit since "[a]t a certain point, the level of 6-TG will be so high and so toxic that it will cause death (so it is not practically possible to have an infinite amount of 6-TG in a patient)." Pltff's Sur-Rebuttal at 3. Plaintiff admits the patents-in-suit contain no upper limit but argues that "it would be improper to read such a limitation into the claim." *Id.* (citing *Gart v. Logitech, Inc.*, 254 F.3d 1334, 1343 (Fed.Cir. 2001)). This Court's review of the patents

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[7] For purposes of these motions, 6-TG (6-thioguanine) and 6-TGN (6-thioguanine nucleotides) are used interchangeably. *See* Pltff's Mot. at 3, n.2.

reveals that plaintiff is correct. No upper limit is mentioned in the patents-in-suit and, thus, such limitation cannot be considered in construing the terms of the patent claims. *See Phillips*, 415 F.3d at 1312-13. Therefore, defendant's argument fails.

The patents-in-suit do not contain an express definition of "greater than." According to plaintiff, the dictionary definition of "greater than," considered along with the intrinsic evidence supports plaintiff's interpretation of the claims. Pltff's Opp. at 14. Plaintiff explains that, when the ordinary meaning of "greater than" is applied, the term means "a level of 6-TGN above 'about 400.'" Pltff's Mot. at 16. Plaintiff notes, in its reply brief, that the inventors used, as an example in the patent specification, a 490 level of 6-TGN found to correlate with hematologic toxicity in adults which "'should be monitored to avoid potential clinical bone marrow suppression.'" Reply at 5 (quoting Bloomfield Decl., Exh. 1 at 32). Plaintiff asserts that the Federal Circuit has found construction of claims that exclude the preferred embodiment is "'rarely, if ever, correct.'" *Id.* (quoting *Interactive Gift Express, Inc. v. Compuserve, Inc.*, 256 F.3d 1323, 1343 (Fed. Cir. 2001)). Plaintiff explains that "greater than" as used in the patents means "[a]ny level that is above [about 400]" and "[a]ny level which is lower than [about 400] is not a level which is greater than [about 400]." Pltff's Sur-Rebuttal at 2. Defendant does not dispute plaintiff's construction nor present its own proposed construction of the term.[8]

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[8] Plaintiff, however, construes defendant's oral argument as presenting a definition of "greater than" which "requires (1) "a comparison of the 6-TG level to 'about 400' and (2) a finding

This Court finds that plaintiff's construction of "greater than" defined as "any level that is above about 400" is a proper construction of the term based on its "ordinary and customary meaning, determined from the view of a person of ordinary skill in the relevant art." *Phillips*, 415 F.3d at 1312-13. Therefore, this Court construes "greater than" to mean any level that is above "about 400."

2. "About 400"

Both parties appear to agree that the patents-in-suit contain no express definition of the word "about" but differ on whether the Court should consult extrinsic evidence to determine its meaning. Defendant urges the Court to construe the word "about" without consulting extrinsic sources. Plaintiff disagrees, contending that, because the word is not expressly defined in the patent, consulting extrinsic evidence is necessary to properly define the word. The *Phillips* court, discussing the use of extrinsic evidence in claims construction, instructs that:

> ... extrinsic evidence may be useful to the court, but is unlikely to result in a

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that the 6-TG level is greater than 'about 400.'" Pltff's Sur-Rebuttal at 7. Although plaintiff's construction of defendant's argument generously provides defendant with a definition of the term, this Court's does not so construe defendant's arguments, written or oral. This Court does not believe defendant intended to present a definition of "greater than" by adding requirements to the term. Even if defendant had so intended, this Court deems it improper to construe a term by adding additional requirements to alter its plain meaning. *See Phillips*, 415 F.3d at 1312-13. Because defendant presents no other possible construction of "greater than," this Court finds defendant does not present its own construction of "greater than" and addresses only plaintiff's proposed construction.

> reliable interpretation of patent claim scope unless considered in the context of the intrinsic evidence. Nonetheless, because extrinsic evidence can help educate the court regarding the field of the invention and can help the court determine what a person of ordinary skill in the art would understand claim terms to mean, it is permissible for the district court in its sound discretion to admit and use such evidence. In exercising that discretion, and in weighing all the evidence bearing on claim construction, the court should keep in mind the flaws inherent in each type of evidence and assess that evidence accordingly.

Id., 415 F.3d at 1319.

Based on case authority defining the word "about" in various contexts, defendant contends that the proper construction of the word "about" requires it be defined narrowly as "with some approach to exactness in quantity, number, or time[,]' 'approximately,' [or] 'reasonably close to.'" Deft's Suppl. Reply at 7 (citing *Merck & Co. v. Teva Pharm. USA, Inc.*, 395 F.3d 1364, 1369-72 (Fed.Cir. 2005) ("about" means "approximately"); *Conopco, Inc. v. May Dep't Stores Co.*, 46 F.3d 1556, 1561 & n.3 (Fed.Cir. 1994) ("the term ['about'] means ... 'with some approach to exactness in quantity, number, or time,'" adopting Webster's Third New International Dictionary definition); *Cellnet Data Sys. Inc. v. Itron, Inc.*, 17 F.Supp.2d 1100, 1114 (N.D.Cal. 1998)("about" means "reasonably close to."); Bush Decl., Exh. W (Order

filed by a Delaware district court, on July 26, 2005, construing "about" in patent as "approximately")).

Plaintiff, on the other hand, points to other cases that indicate the word "about" actually broadens the number, creating a range dependent upon the precision of measurement for the particular technology. Pltff's Suppl. Opp. at 7 (citing *Pall Corp. v. Micron Separations, Inc.*, 66 F.3d 1211, 127 (Fed. Cir. 1995) ("the use of the word 'about,' avoids a strict numerical boundary to the specified parameter."); *Modine Mfg. Co. v. U.S. Int'l Trade Commission*, 75 F.3d 1545, 1554 (Fed. Cir. 1996) ("about" is a "broadening usage[]" which is given a "reasonable scope" and depends on the context and precision of measurement error for the claimed technology)). Plaintiff notes that some courts have actually construed "about" to encompass much broader ranges than the cases cited by defendant. *Id.* at 7, 8 n.6 (citing, *inter alia*, *Hybritech Inc. v. Abbott Labs*, 849 F.2d 1446, 1455-56 (Fed. Cir. 1988) (using a two to three fold error in measuring antibodies); *Schreiber Foods, Inc. v. Saputo Cheese USA Inc.*, 83 F.Supp.2d 942 (N.D. Ill. 2000) (construing "about 2 minutes to about 4 minutes" as encompassing 30 seconds to ten minutes and "about 190 degrees to about 205" as including 150 to 300 degrees)).

Although defendant argues, during oral argument, that no specific range of numbers should be used in defining "about 400," plaintiff contends the proper construction of "about 400" is a range of "400 +/-15-20%," based on extrinsic sources. *See* Pltff's Suppl. Opp. at 8-13. Plaintiff points to various sources of extrinsic evidence, including the Food and Drug Administration ("FDA") guidelines, scientific

articles, defendant's documents, expert testimony, and the inventors' testimony, in support of the broader interpretation. *See id.* at 10-13. Plaintiff explains the FDA guidelines are useful in determining what a person of ordinary skill in the art would understand the word "about" means, as used in the patents-in-suit. *Id.* Plaintiff claims that the Federal Circuit "*expressly approved*" the use of FDA guidelines in claims construction and decision in *Phillips* did not alter that approval. *Id.* (emphasis in original) (citing *Key Pharm. v. Hercon Labs Corp.*, 161 F.3d 709, 718 (Fed. Cir. 1998) ("it is quite sensible to look to the FDA" guidelines on measurements in order to properly construe a claim term.)). Plaintiff points out the FDA guidelines provide a standard for precision and accuracy in blood testing of +/- 15% or, at the lowest level of detection, 20%. *Id.* at 4 & n.4. Plaintiff notes that the appropriate variation for the patented test is 15% because the lowest level of detection, considered the most imprecise level warranting a 20% variation, is not applicable here. *Id.* Thus, plaintiff contends a person of ordinary skill in the art would understand "about 400" to mean "400 +/-15%." *Id.* at 4-5.

In its rebuttal brief, defendant urges the Court to discount the FDA guidelines' usefulness here[9] be-

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[9] Defendant does not appear to dispute that the 2001 guidelines are the applicable guidelines for the patents-in-suit. This Court notes that the FDA implemented the guidelines in 2001 based on the deliberations of two prior workshops held in 1990 and 2000. *See* Morgan Decl., Exh. 6 at 624. This Court's independent research reveals no earlier edition of FDA guidelines existed at the time the 2001 guidelines were issued. Thus, this Court finds the 2001 FDA guidelines are properly applicable to the instant patents.

cause "[t]hey generally establish outer limits for acceptability for the measurement of metabolite levels under a wide variety of circumstances, including measurements in animals" and "say nothing about the actual precision of tests measuring 6-TG or 6-MMP." Deft's Rebuttal at 5-6. Defendant suggests, instead, that the Court look to "the only record evidence regarding the actual precision of tests measuring" these metabolites – defendant's accused test, which lists a precision of 1.5 - 3.8%. *Id.* at 6. Plaintiff, in response, contends defendant's suggestion to use its own test's precision rate is "absurd" because the accused test was developed well after the patents-in-suit were filed. Pltff's Sur-Rebuttal at 4, n.3. Plaintiff argues that to do so would be clear error. *Id.* (citing *SRI International v. Matsuchita Elec. Corp. of America*, 775 F.2d 1107, 1118 (Fed.Cir. 1985)).

This Court finds defendant's proposed definitions of "about" to mean "with some approach to exactness in quantity, number, or time," "approximately" and "reasonably close to," although extracted from case authority, are too vague to be useful in the context of the metabolite measurements at issue here. These definitions fail to impart a specific numerical range a person of ordinary skill in the art would understand equates to a metabolite level of "about 400." In fact, defendant admits, during oral argument, that its construction does not does not delineate a specific numerical range, but contends the Court is not required to do so in order to properly construe the claim term. This Court is unconvinced that a person of ordinary skill in the art would define "about 400" without determining a specific numerical range encompassing the amount. Accordingly, this Court deems it appropriate to resort to extrinsic evi-

dence to determine the specific numerical range imparted by the term "about 400" as a person of ordinary skill in the art would understand it.

As noted previously, defendant presents no extrinsic evidence to aid in the Court's claims construction. Plaintiff, on the other hand, presents various sources of extrinsic evidence, including declarations of expert witnesses and the inventors of the patents-in-suit, as well as a variety of documentary evidence. This Court is mindful that the declarations of expert witnesses and the inventors are, for the most part, to be viewed cautiously because such evidence is "generated at the time of and for the purpose of litigation and thus can suffer from bias." *Phillips*, 415 F.3d at 1318. However, this Court finds that consideration of the declarations submitted by plaintiff are not necessary to properly construe the claim term at issue. Thus, the declarations of expert witnesses and the patent inventors will not be considered.

Plaintiff relies heavily upon the FDA guidelines to support its proposed construction. This Court is unpersuaded by defendant's characterization of the FDA guidelines as unreliable because they establish general guidelines used in a variety of areas and are, therefore, not specific guidelines for measuring the metabolites involved in this suit. Defendant's suggestion to use the accused test's stated accuracy rate instead is, in this Court's view, inappropriate because the test was developed after the '623 patent was filed and the FDA guidelines were issued.[10]

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[10] This Court notes that the only evidence presented by defendant of the claimed accuracy rate of its accused test comes from the deposition testimony of a physician (apparently an expert

As plaintiff notes, the Federal Circuit agrees the FDA guidelines may be useful in claims construction. *See Key Pharm.*, 161 F.3d at 718. This Court finds the FDA guidelines useful here. This Court deems the FDA guidelines reliable, in that they can be considered in the same genre as dictionaries and treatises since they do not suffer from the bias expert witness testimony presents. The *Phillips* court expressly approved the use of dictionaries and technical treatises in claims construction as long as "'the dictionary definition does not contradict any definition found in or ascertained by a reading of the patent documents.'" *Id.*, 415 F.3d at 1322-23 (quoting *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1584 n.6 (Fed.Cir. 1996)).

In that vein, defendant contends that the patent specification contains references to various other levels mentioned in prior art which were not claimed in the patents-in-suit.[11] According to defendant, the patent specification of both patents-in-suit state that, in addition to an "about 400" toxicity level for 6-TGN,

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witness), which is the type of evidence the *Phillips* court found to be extremely unreliable. *See Phillips*, 415 F.3d at 1318.

[11] Defendant also contends plaintiff's proposed construction would render the patents invalid for indefiniteness because the construction "does not provide the public with adequate notice of what the range of 'about 400' covers." Deft's Suppl. Reply at 10. Claims are indefinite if they do not "adequately notif[y] the public of the patentee's right to exclude." *Honeywell Intern., Inc. v. I.T.C.*, 341 F.3d 1332, 1338 (Fed. Cir. 2003). However, as plaintiff correctly notes, it is improper to consider patent validity in determining claim construction unless the patent claims are found to be ambiguous, which is not the case here. *See* Pltff's Reply at 8-9 (citing *Phillips*, 415 F.3d at 1327).

levels "'also can be about 350 pmol[12] per $8x10^8$ RBC, 370 pmol per $8x10^8$ RBC, 390 pmol $8x10^8$ RBC, 425 pmol per $8x\ 10^8$ RBC; or 450 $8x\ 10^8$ RBCs.'" Deft's Mot. at 20 (quoting Bush Decl., Exh. A at 12 & Exh. G at 13). Thus, defendant argues those claimed levels are dedicated to the public [13] and cannot now be claimed by the patentees. Defendant contends the patent applicants presented arguments to the patent office indicating the toxicity level described in prior

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[12] The letters "pmol" is an abbreviation for the word picomole, which is a unit of measurement for metabolites used in medical tests. In the Sanborn patent, levels of 6-TGN and 6-MMP are expressed in terms of how many picomoles are in every 10^8 red blood cells while the patents-in-suit levels are expressed in terms of how many picomoles are in every $8x10^8$ red blood cells. Defendant claims that Dr. Sandborn's use of 10^8 (or 100,000,000) instead of $8x10^8$ (or 800,000,000) "is clearly a typographical error" in the earlier patent. *See* Deft's Mot. at 4-5. However, plaintiff notes that what defendant "believes" is "irrelevant" because Dr. Sandborn's patent uses 10^8 red blood cells and no attempts to correct what defendant believes is a mistake have been made. Pltff's Opp. at 14, n.4. This Court finds it inappropriate to interpret or construct the terms contained in the Sanborn patent to correct alleged errors because such interpretation is immaterial to the resolution of the issues here. Thus, this Court declines to resolve the issue.

[13] Plaintiff disputes defendant's use of the doctrine of dedication to the public in the context of claims construction because the doctrine has only been applied as a defense to liability for infringement based on the doctrine of equivalents. *See* Pltff's Sur-Rebuttal at 13. The argument presented by defendant is that plaintiff disclosed the claimed levels in the patent specification but did not claim them in the patent, thereby rendering the disclosed levels available for public use. Defendant's public use argument is similar, but not identical, to the doctrine of dedication to the public referred to by plaintiff and is, in this Court's view, a valid argument in determining claims construction.

art differed from the patents-in-suit's level recited in the patents. *Id.* at 20 (citing Bush Decl., Exh. K at 16, Exh. O at 4, Exh. N at 13). Defendant argues that "what was different, and new, about their 'invention' was the specific levels of 6-TGN and 6-MMP recited in their claims." Deft's Reply at 3. Therefore, defendant contends that "about 400" cannot encompass any of the levels disclosed in the patent specification because those levels have been dedicated to the public.

In response, plaintiff contends that "the phrase 'about 400' denotes the lower limit of a range of 6-TGN values beginning at 400." Pltff's Opp. at 15. Plaintiff claims that the portions of the specification defendant refers to are actually consistent with plaintiff's construction "because the specification explicitly states that a 'predetermined toxic level' is not an exact number but rather a range." Pltff's Reply at 6. Thus, according to plaintiff, the ranges mentioned in the specification are different ranges than "about 400" but overlap. *Id.* at 9-10.

As to defendant's argument that plaintiff disavowed the disclosed levels during prosecution, plaintiff points out that statements made during prosecution will not disclaim the scope of the claim absent a clear and unequivocal disavowal by the applicant, which did not happen here. *Id.* at 7 (citing *IMS Tech., Inc. v. Haas Automation, Inc.*, 206 F.3d 1422, 1433-34 (Fed. Cir. 2000); *Aquatex Indus., Inc. v. Techniche Solutions*, 419 F.3d 1374, 1382-83 (Fed. Cir. Aug. 19, 2005)). Plaintiff observes that the Federal Circuit warned a patent's prosecution history may not be useful in claim construction because "'it represents an ongoing negotiation between the PTO

and the applicant, rather than the final product of that negotiation.'" *Id.* (quoting *Phillips*, 415 F.3d at 1317). Plaintiff contends that, in this case, no "clear and unequivocal" disavowal of the disclosed levels was expressed during prosecution of the patents and, thus, no disclaimer of that level can now be found. *Id.* at 7-8.

This Court's review of the record reveals plaintiff did not clearly and unequivocally disavow the disclosed levels in the patents. Although the patent applicants disclosed various levels during prosecution, the levels were disclosed by stating that the levels "can also be about 350 pmol ..." *See* Bush Decl., Exh. A at 12. This Court is not persuaded that prefacing disclosures with "can also be" may be considered a clear and unequivocal disavowal of the subject matter. This Court has found no indication in the intrinsic record that the disclosed levels were clearly and unequivocally disavowed by the patent applicants. Therefore, the patentee's disclosure and failure to claim the levels does not operate as a disclaimer of the use of those levels. *IMS Tech*, 206 F.3d at 1433-34; *Aquatex*, 419 F.3d at 1382-83. This Court thus finds the range of "about 400" may properly encompass the disclosed levels.

A careful review of the intrinsic record has discovered no other language that might contradict plaintiff's proposed definition of "about." Therefore, based on the reliable extrinsic evidence provided by plaintiff, this Court finds that the term "about" means "+/- 15%" based on its "ordinary and customary meaning, determined from the view of a person of ordinary skill in the relevant art." *Phillips*, 415 F.3d at 1312-13. Accordingly, "about 400" is construed as

400 +/- 15% encompassing a numerical range of 340 to 460.

b. "Indicates a Need"

Plaintiff also contends that the term "indicates a need" as used in the patents-in-suit should be properly construed in order to determine infringement in this case. According to plaintiff, "indicates a need" is "a marker or warning that one should decrease [the] next dose of [the] drug administered" but does not require an actual decrease to occur. Pltff's Mot. at 17-18. Plaintiff claims that the patent specification, the prosecution history and extrinsic evidence supports this ordinary meaning. *Id.* at 18-21 (citing Bloomfield Decl. ¶¶ 38-47, Exh. 1 at 4, 8, 12, Exh. 3 at 284, 298-98, Exhs. 8-11, 20).

Defendant, in opposition, points out that plaintiff's proposed construction "reads the word 'need' right out of this phrase and even ignores the very dictionary definition of 'need' [plaintiff] cites in its brief." Opp. at 18. Defendant contends the intrinsic record precludes plaintiff's construction of this phrase. *Id.* According to defendant, the parties agree that "need" is defined as "a necessary duty or obligation." *Id.* (citing Morgan Decl., Exh. 16; Pltff's Mot. at 18). Defendant argues "indicates a need" can only mean "indicates a necessary duty or obligation." *Id.* Thus, defendant asserts the patent claims "require that the metabolite levels 'indicate a necessary duty or obligation to decrease the amount of said drug subsequently administered' – i.e., an infringing test must advise doctors to lower the amount of drug if the predetermined toxic level is exceeded." *Id.* Defendant argues that plaintiff's construction, substituting "should" for "must," flies in the face of the de-

finition of "need" presented in plaintiff's moving papers. *Id.* Defendant also points to the patent specification and the prosecution history in support of its construction. *Id.* at 19-20 (citing Bush Decl., Exh. A at 18; Exhs. L at 7, Z at 18, AA at 4). Defendant claims it is unnecessary to resort to extrinsic evidence to construe the terms. *Id.* at 22.

In reply, plaintiff disagrees with defendant's interpretation of "indicates a need," claiming defendant's proposed construction requires an actual lowering of the drug dosage if the test shows a metabolite level greater than about 400, when, in fact, the claim does not so state. Pltff's Reply at 10-11. Plaintiff points out that the inventors used the term "adjusting" in the specification but did not include the same term in the claim, even though they could have done so. *Id.*

Plaintiff contends the results of the patented test are merely one factor to be considered in adjusting dosage; the patented test does not require subsequent doses actually be lowered as defendant agues. *Id.* Plaintiff also contends that defendant's construction of "indicates a need" fails to give meaning to the word "indicate" and adds an additional requirement that doses actually be adjusted that is not part of the claim. *Id.* at 11. Plaintiff argues that such claim construction is improper. *Id.* (citing *Texas Instruments, Inc. v. U.S. Int'l Trade Comm'n*, 988 F.2d 1165, 1171 (Fed. Cir. 1993)(cautioning that every word in a claim must have meaning); *Interactive Gift*, 256 F.3d at 1335 (warning that limitations cannot be imported from the specification or prosecution history into the claims); *Gart v. Logitech, Inc.*, 254 F.3d 1334, 1343 (Fed. Cir. 2001)(same)). Finally, plaintiff points out

that the specification and prosecution history do not indicate a deviation from the clear language of the claims that defendant's interpretation requires. *Id.* at 12-13.

This Court agrees with plaintiff. In this Court's view, "indicates a need" suggests to the doctor reviewing the test that an adjustment in dosage may be required. This Court is unpersuaded by defendant's argument that the word "need" signifies the patented test requires doctors to adjust drug dosage if the metabolite level reaches the specified level. There is nothing in the patent specification or prosecution history that leads this Court to believe that such a requirement should be found. Because "need" is prefaced by "indicates," this Court finds the phrase means that when the identified metabolites reach the specified level, the doctor is warned or notified that a dosage adjustment may be required, if the doctor believes that is the proper procedure. Accordingly, this Court, based on the "ordinary and customary meaning, determined from the view of a person of ordinary skill in the relevant art," construes "indicates a need" to mean "a warning that an adjustment in dosage may be required." *Phillips*, 415 F.3d at 1312-13.

3. Conclusion

Based on the foregoing, this Court construes the following terms contained in the patents-in-suit:

1. "Greater than about 400" is construed to mean "any level above 340 to 460;" and

2. "Indicates a need" is construed to mean "a warning that an adjustment in dosage may be required."

B. Infringement

1. Legal Standard

Once the claim terms are properly construed by the court, the properly construed claims "must be compared to the accused device or process." *C.R. Bard, Inc. v. United States Surgical Corp.*, 388 F.3d 858, 861 (Fed. Cir. 2004). To infringe a patent, a patentee must prove the accused device meets each claim limitation, either literally or under the doctrine of equivalents.[14] *Liquid Dynamics Corp. v. Vaughn Co.*, 355 F.3d 1361, 1367 (Fed. Cir. 2004).

2. Analysis

Defendant, in its summary judgment motion, seeks a declaration of non-infringement. Contrarily, plaintiff, in its cross-motion for summary judgment, contends that the accused test literally infringes claim 7 of the '623 patent. To establish literal infringement of a patent "every limitation [or element] set forth in a claim must be found in an accused

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[14] Defendant presents various arguments, in its moving papers, concerning infringement based on the doctrine of equivalents, contending that the doctrine does not apply in this case. *See* Deft's Mot. at 23-25. In opposition to defendant's motion, plaintiff argues that the doctrine of equivalents does apply. *See* Pltff's Opp. at 19. However, plaintiff's cross-motion for summary judgment, seeking a declaration of infringement, is based solely on literal infringement of Claim 7 of the '623 patent. *See* Pltff's Reply at 10. Accordingly, this Court addresses the parties' arguments concerning literal infringement only and does not address arguments concerning the doctrine of equivalents, including defendant's arguments regarding the doctrine of dedication to the public or prosecution history estoppel.

product or process." *Johnston v. IVAC Corp.*, 885 F.2d 1574, 1577 (Fed. Cir. 1989). "There can be no infringement as a matter of law if a claim limitation is totally missing from the accused device." *London v. Carson Pirie Scott & Co.*, 946 F.2d 1534, 1538-39 (Fed. Cir. 1991).

Defendant describes its accused test as follows:

> the accused test measures levels of 6-TGN and 6-MMP in a patient's blood, and reports these results to a treating physician. With these results, the test includes the following information:
>
> > [L]evels of 6-TGN . . . greater than 450 pmol/8x10^8 cells may be associated with increased risk of myelosuppression, liver injury, pancreatitis, and allergic reactions.
> >
> > . . .
> >
> > 6-MMP levels of >5700 pmol/8x10^8 RBC have been reported to be associated with an increased frequency of abnormal liver function tests.

Deft's Mot. at 5 (quoting Bush Decl., Exh. E at 2). Thus, the accused test informs physicians that, when metabolite levels reach 450 and above, possible complications may occur. However, the test states that "a

clearly defined toxic level has not been established." Bush Decl., Exh. E at 2.

Plaintiff argues that defendant's proposed test, announced in its implementation notice dated June 9, 2004 (thus constituting an offer for sale[15]), literally infringes plaintiff's patents because the accused test:

> Meets every limitation of the method of claim 7: (1) the administration of a drug providing 6-thioguanine to a subject having said immune-mediated gastrointestinal disorder; (2) determining the level of 6-thioguanine in said subject and determining the level of 6-methylmercaptopurine in said subject; and (3) wherein the level of 6-thioguanine greater than about 400 pmol $8x10^8$ red blood cells indicates a need to decrease the amount of said drug subsequently administered to said subject.

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[15] The parties do not appear to dispute that defendant's announcement constitutes an offer for sale. An offer for sale of a patented invention by one who is not the patent owner or licensee may constitute infringement. *See* 35 U.S.C. § 271(a). Defendant argues that, because the claims in the patents-in-suit are method claims, the claims may only be infringed if the method is actually performed. Deft's Opp. at 24 (citing *Joy Technologies v. Flakt, Inc.*, 6 F.3d 770, 773 (Fed. Cir. 1993)). Defendant notes that it has only offered its test for sale and, thus, has not actually performed the test. *Id.* at 24-25. However, plaintiff, in reply, correctly points out that the statute governing patent infringement (amended after the *Joy* case, which does not involve an offer for sale) clearly states that an offer for sale creates liability for infringement. Pltff's Reply at 14, 22 (citing 35 U.S.C. § 271(a)). Therefore, defendant's argument fails.

Pltff's Mot. at 23 (citing Bloomfield Decl. ¶¶ 48-54). Plaintiff claims that defendant's accused test clearly meets the first two limitations. *See id.* at 23-24. As to the third limitation, plaintiff contends that the accused test infringes when the claim terms are properly construed as previously argued. *Id.* at 24-25.

Defendant contends, in opposition, that the accused test, if used, would not infringe the patents-in-suit for two reasons: (a) the test would not use either claimed level of "about 400" or "about 7000;"[16] and (b) the test would not "indicate a need to decrease the amount of said drug subsequently administered" to a patient. *Id.*

a. Use of "about 400"

Defendant argues, in opposition, that a proper construction of the claim terms "greater than" and "about 400" using defendant's proposed construction would render defendant's accused test not infringing plaintiff's patents. Deft's Opp. at 22. However, this Court has now adopted plaintiff's construction of the

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[16] Defendant points out that plaintiff has failed to present evidence proving the accused test uses the level of "about 7000." Deft's Opp. at 22. Defendant contends that Claim 7 of the '623 patent requires that both levels be used "as a 'double-check' against toxicity," and defendant's accused test uses neither. *See* Deft's Rebuttal at 4-5. Plaintiff, in response, explains that Claim 7 provides for "alternative levels that serve as an indication of a need to decrease doses." Pltff's Sur-Rebuttal at 1 (emphasis omitted). This Court's review of the patent language reveals that plaintiff's interpretation is correct. Although both levels may be measured to determine whether dosage adjustment is needed, the physician is notified if either level exceeds the predetermined toxic level. Accordingly, defendant's argument that both levels must be used by the accused test in order to find infringement is without merit.

claim term "greater than," construing the term to mean "any level above" the specified level. The accused test uses a metabolite level of 450 which is clearly above the "about 400" level. This Court has also adopted plaintiff's construction of "about 400," construing the term to mean "400 +/- 15% or a range of 340 to 460." The accused test's level falls within that range also. Thus, the accused test literally infringes the "greater than about 400" element of the patented test.

b. "Indicates a Need"

Defendant also contends that a proper construction of "indicates a need" would obviate any infringement because its accused test as described in the implementation notice does not inform the physician that the dosage should be changed. Deft's Opp. at 23. Instead, defendant argues that the notice informs physicians of "possible myelosuppression" which indicates the physician should consider the possibility that there is toxicity without providing a possible action to take. *Id.* (citing Bush Decl., Exh. S at 57, 61). In addition, defendant explains that the accused test would include cautionary language informing doctors to "monitor white cell count to detect myelotoxicity ... and ... TGN concentrations" and stating "that there is no defined toxic level established." *Id.* at 24 (quoting Bush Decl., Exh. S at 147; citing Bush Decl., Exh. CC). Thus, defendant contends that the 6-TGN levels are merely one factor doctors consider in treatment based on defendant's accused test's results, which does not meet the "indicates a need" prong in plaintiff's patents. *Id.*

This Court has now construed "indicates a need" to mean "a warning that an adjustment in dosage may be required." Defendant's explanation of the accused tests' procedure appears almost identical to this Court's view of the patented test's procedure. The accused test, used for patients taking AZA drugs, informs physicians that metabolites measuring above the levels stated have been known to cause certain effects, which information the doctors may use to determine further treatment. The patented test warns physicians that, when metabolite levels reach above a certain point, an adjustment in dosage may be warranted. This Court notes that both tests are used in measuring the metabolite level in patients taking AZA drugs and inform physicians that the higher metabolite level raises the risk of toxic side effects. Defendant's test may not actually state that drug dosage should be reduced, but the fact that the accused test measures the metabolite level of patients taking AZA drugs implies that, when the risk of toxic side effects are raised, drug dosage adjustment may be one of the proper courses of action to avoid toxic side effects of the drugs. That is exactly what plaintiff's patented test warns. Therefore, this Court finds defendant's accused test literally infringes the "indicates a need" element of the patented test.

3. Conclusion

Based on the Court's construction of the claim terms at issue, and for the reasons presented, this Court finds that there is no genuine issue of material fact to be resolved as to whether defendant's accused test literally infringes plaintiff's patents. This Court finds defendant's accused test literally infringes all

elements of the patents-in-suit. Because this Court has ruled in plaintiff's favor on the issue of infringement, plaintiff's Rule 56(f) motion for further discovery on that issue is moot.

CONCLUSION AND ORDER

Based on the foregoing, IT IS HEREBY ORDERED that:

1. Defendant's motion for summary judgment is **DENIED**; and

2. Plaintiff's cross-motion for summary judgment is **GRANTED**.

IT IS FURTHER ORDERED that defendant's motion to strike plaintiff's objections to defendant's facts and evidence [doc #73] and plaintiff's request for further discovery pursuant to Fed.R.Civ.P. 56(f) are **DENIED as moot.**

Dated: November 21, 2005

/s/
JOHN A. HOUSTON
United States District Judge

cc: Magistrate Judge Brooks
All Counsel of Record

APPENDIX D

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF CALIFORNIA

Civil No. 04cv1200 JAH (RBB)

PROMETHEUS LABORATORIES, INC.,
Plaintiff,

v.

MAYO COLLABORATIVE SERVICES dba MAYO MEDICAL LABORATORIES and MAYO CLINIC ROCHESTER,
Defendants

AND RELATED COUNTERCLAIM.

FINAL JUDGMENT

Pursuant to Federal Rule of Civil Procedure 54 and the parties' stipulation, it is hereby adjudged, ordered and decreed that:

1) The Court's March 28, 2008 Order Granting Defendants' Motion for Summary Judgment of Patent Invalidity Pursuant to 35 U.S.C. § 101 is a final judgment against Prometheus Laboratories, Inc. in this action;

2) Each and every remaining claim and counterclaim of Prometheus Laboratories Inc. is voluntarily dismissed without prejudice;

3) Each and every remaining counterclaim of defendants Mayo Collaborative Services dba Mayo Medical Laboratories, and Mayo Clinic Rochester

("Defendants") is voluntarily dismissed without prejudice;

4) Each party will bear its own fees and costs.

The clerk is directed to enter this judgment forthwith.

Dated: May 16, 2008

/s/
JOHN A. HOUSTON
UNITED STATES
DISTRICT JUDGE